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CLINIC OF DR. C. C. BASS

NEW ORLEANS, LA.

## PELLAGRA

OUR presentation this morning will be based upon a case of pellagra that has been worked up and presented in class work by one of the senior students, and upon 2 cases of the same disease in physicians seen by me many years ago, who recovered from rather severe attacks and are still living.

These cases will serve to illustrate certain interesting features as to the nature and cause of this mysterious disease, the specific cause of which still remains to be discovered.

The first case is that of a negro woman from Crowley, Louisiana, aged thirty-two, married, two children. She has lived in the country all her life and has worked in the rice fields for many years. The present illness began about one and a half months ago, and has grown progressively worse until the present time.

According to the history, this woman washed clothes in the sunshine one day and complained that the soapy water and hot sunshine together caused her hands and forearms to burn and sting, although there was nothing else noticeable about them. They kept stinging and burning, and also the skin over the front of her neck. Within two or three days they became darker than the other parts of her body. The history goes on to describe the development and course of typical, rather severe pellagrous lesions on her hands, including the backs of the fingers, around the wrists, and on the forearms, and also on the neck, extending down in front over the sternum, V shaped, corresponding to the opening of her dress (Casal's collar).

These lesions passed through the usual stages of erythema, vesication, and scaling. There were somewhat milder lesions on the tops of the feet.

Although the pellagrous lesions that developed first have greatly improved, there are two noteworthy conditions to which I wish to direct attention. One of these is the thickened, hard, and very rough skin over the nose, especially the sides, the chin, and, to a less extent, the forehead. No erythema or exfoliation occurred, and there was little or no change of color.

I have often noticed this condition of the skin of the face, particularly in severe cases of pellagra in negro women. The skin becomes thick and hard. When asked about it, the patient may note a feeling of numbness and stiffness. Hardened sebaceous material protrudes from the sebaceous glands where these are most numerous and active, as on the sides of the nose, and on the chin of "greasy-faced" negroes, giving to the skin a very rough grater-like feel.

The other skin lesions to which attention is directed consist of severe lesions on the points of the elbows. The lesions on the hands, neck, and feet ran the usual course for such lesions, but a few days after the patient was admitted to the hospital she developed a large severe lesion on the right elbow from which the skin slipped off, leaving it raw and bleeding, and a smaller, less severe, very dark lesion on the left elbow. These lesions on the elbows developed nearly a month after the first lesions on the hands began and only after the patient's general condition became so bad that she was confined to bed and her mental condition became so poor that she became awkward and did not exercise the usual care against abuse of herself in moving around in bed, especially in getting up and down. It often occurs that pellagra patients develop lesions on the elbows as soon as they are confined to bed. A large proportion of the acute very active cases develop such lesions, especially those whose nursing and care are such as to allow them to rise and rest upon their elbows in bed.

The lesions in pellagra are caused by physical forces or chemical action on the skin in persons whose skin has lost its

normal ability to resist such action as a result of the disease. Pellagra is a general disease, and not merely a skin disease, as the prominence and frequency of the skin lesions may suggest.

It seems that lesions are produced only when the cause is active at the proper stage and period of activity of the general disease. At other times, in milder cases and during a period of general improvement, the same influences do not bring out lesions.

The first case of pellagra I ever saw to recognize presented the most convincing evidence of the influence of direct exposure to hot sunlight in the development of the skin lesions. The patient had been sick with "indigestion, weakness, and nervousness" for a short time, and, upon the advice of her physician, her husband took her for buggy rides in the sun with the hope that this would help her to regain her strength. Severe erythema appeared on both hands and arms up to the part covered by the sleeves. The picture was that of perfectly typical "text-book" pellagra lesions followed by much exfoliation. I saw the patient about two weeks from the time the lesions began, and when there was still very marked erythema, discoloration, and exfoliation. The lesions involved the backs of the fingers, less over the first phalanges. The skin over the third phalanges was involved almost as much as the backs of the hands except for a wide band on the ring-finger of the left hand, which was perfectly clear. They stated that she wore a wide band ring on this finger constantly, including the time when she was exposed to the hot sunshine just previous to the development of the lesions. I shall never forget the sharp contrast in the appearance of the skin above and below, with the perfectly normal appearance of the band that had been covered by the ring, and thereby protected from the sun.

This evidence was most convincing that these lesions were caused by exposure to direct sunlight in a patient whose skin was susceptible to such effect and, further, that protection from sunlight prevented development of the lesion on an area that was otherwise susceptible. Could there be any reasonable doubt that if all the skin of the hand, or of both hands, had been protected from the sun as thoroughly as this band around the finger,

no lesions whatever would have developed? I say there could not be, nor could there be any reasonable doubt that if the band had not been protected the lesion would have developed there as it did above and below on the same finger and on corresponding areas on the other fingers.

It is quite likely that exposure to sunshine of certain quality or intensity that may not now be understood may be most effective in producing the lesions on the skin of a person who has the general disease at the stage which renders him susceptible.

Although exposure to sunshine in some way is the exciting cause of the lesions in most cases, there are several other things that we know of that may cause them and, no doubt, others that we do not know of. Exposure to heat will cause them, as in the case of a woman whom I once saw who developed severe lesions chiefly on the lower or ulnar side of the forearms following cooking and working for hours over a hot stove at the time she was already sick, probably from the early general effect of pellagra.

Such things as pressure and trauma to the skin may cause the development of lesions as occur on the elbows of patients who are confined to bed, especially if there is more or less dementia, as in the case of our negro woman. In most very acute fulminating cases lesions develop on parts where there is pressure, such as over the heels or the bony prominences on the back, shoulders, etc.

Irritating chemicals may cause lesions to develop. Strong ointments containing such agents as carbolic acid, ichthyol, and iodin, when applied to pellagrous lesions, not only make them much worse, but tend to make them spread as far as the ointment is applied beyond the lesion. I have seen lesions under the pendulous breasts of a fat woman caused by irritating, sour, unclean perspiration. The same woman had typical lesions on her hands on which the diagnosis of pellagra was based.

The mucous membranes are susceptible to irritating influences in much the same way as the skin. The vaginitis and vulvitis so frequently occurring in women with pellagra result from the effect of irritating acrid vaginal discharges, against which the tissues of a normal person are more resistant.

I think it quite likely that the gastric disturbance, the diarrhea so often present, and the irritation and inflammation of the intestinal mucosa found at autopsy are the result of the effect of the digestive juices on these tissues which normally are not effected by them.

Our negro woman had diarrhea, emaciation, sore tongue, etc., which usually occur in such cases and require no special comment. There is a feature in the history, however, which is especially noteworthy in connection with our previous discussion of the manner in which the lesions are excited by conditions or influences that may or may not exist in every case. She has shown more or less dementia all the time she was in the hospital. She constantly wants to leave the hospital because she is "afraid she is going to be drowned." However, her mental condition does not seem to be any worse than may be expected in such a case.

The interesting feature shown by the history in this connection is that, although she and her sister with whom she lives say that she never had any such condition as the skin lesions she now has, about two years ago she became demented, acted strangely, and her sister stated that she attempted to commit suicide by drowning. Her mental condition was such that sending her to the insane asylum was being considered. This mental derangement lasted for two or three months and then slowly cleared up. They say that she had diarrhea at that time.

Although such a history is likely to be unreliable, it is not at all unlikely that at that time she had the general disease pellagra in which the mental symptoms were most marked, but for some reason no skin lesions developed, without which a definite diagnosis cannot be made. The reason for the development of a good many cases of pellagra in hospitals for the insane may be that the mental condition for which they were sent to the institution was caused by the general disease pellagra, which had not been recognized because the skin lesions on which certain diagnosis rests had not developed.

One of the two physicians to whom I wish to refer briefly brought his brother-in-law to me for consultation. This was the

second case of pellagra that I have any recollection of ever seeing. This was some two years before pellagra was first diagnosed in New Orleans, and, as I recall the case, it was quite typical and presented a clear picture of the disease. The patient was taken to a leading dermatologist, and to a leading psychiatrist, but neither of them thought of pellagra, nor did I.

Some three years later the physician himself began to have rather vague ill health, including especially digestive disturbances, "nervousness," insomnia, hallucinations, weakness, and some loss of weight. He was troubled with sore tongue which he attributed to chewing tobacco. This condition continued for more than a year, better at times, and worse at others.

Following a period of three or four weeks during which he was confined to bed, or to the house most of the time, he got what he first thought was sunburn on his hands as a result of exposure to bright sunshine while riding horseback. This developed to typical pellagrous lesions upon which we were now able to make the diagnosis with certainty, since we had had our attention called to the disease, and had learned to recognize it.

After a few months during which the patient had a rather "rocky time," he went to Colorado, where he slowly improved so that he was able to return to his home in Mississippi, where he is still living and practising medicine, never having had pellagrous lesions again.

The feature in this case to which I wish to direct attention is the evident existence of the general disease pellagra for more than a year before skin lesions developed on which the diagnosis could be made. The necessary combination of the requisite stage or period of the disease with the requisite exciting cause had not existed previously.

The question may be asked why exposure to sunshine had not previously brought out the lesions. I do not wish to convey the idea that exposure to sunshine produces lesions in pellagra patients at any time that it occurs. It is only at certain times, under certain circumstances not now understood, that it will produce them.

The other physician was also from Mississippi. In the sum-

mer of 1911, after a few weeks of "poor health," he developed definite pellagrous lesions on his hands, accompanied by sore tongue, diarrhea, etc. He too was advised to go to Colorado on the theory that since pellagra is a disease of hot regions and most severe during the hot season, it might be improved by a change to a cold climate. After more than two years in Colorado he returned, and has remained in good health and is still engaged in active practice.

These cases, and many more observations which others as well as myself support, the view that the lesions of pellagra may be produced by different agencies in persons whose tissues (skin and mucous membranes) have not the resistance that normal tissues have, and that the lesions are produced merely incidentally or, may I say, accidentally in persons who have the general disease.

It is "anybody's guess" as to what is the specific cause of pellagra. All the evidence of which I have personal knowledge, to which I am able to attach much weight, favors the opinion that it is due to an infection. I am content to remain with the minority who have not been convinced by supposed proof of other causes, and still believe that a specific infection will be found to be the true cause.

## CLINIC OF DR. E. BATES BLOCK

ATLANTA, GA.

### A CASE OF DYSTROPHIA ADIPOSOGENITALIS WITH DISAPPEARANCE OF THE TESTES

DYSTROPHIA adiposogenitalis is sufficiently uncommon to warrant reporting. The following case showed an entire disappearance of the testes which I have not been able to find reported in any other case.

The patient when first seen was eight years and three months old.

*Chief Complaints.*—Trouble in talking; blinking of eyes; very fat.

*Family History.*—Father died aged twenty-nine years, cause unknown; sick only a few days; had purple spots over whole body. Mother living and well. Two brothers living and well, ages nine and eleven years. Mother had had no miscarriages. One maternal aunt died of tuberculosis. Malignancy negative. No nervous or mental diseases. Mother's weight 178 pounds. Height 5 feet, 2 inches. Weighed 93 pounds when she married at age of twenty-five years; weighed 140 pounds fifteen months after marriage. Father died three months before the birth of the patient, and mother was under great mental and physical strain. Father had duodenal ulcer.

*Past History.*—Born at full term. No instruments; not jaundiced. Weighed 7 pounds at birth. Sat alone at six months. Cut teeth normally. Walked at age of two years—crawled at normal age. Had whooping-cough at four years. Fell two years ago and hit against bed-post, striking the back of left side of head—not unconscious. Knot about size of small hickory nut there still, and it gets very red when patient is hot. Much earache before removal of tonsils. Both ears discharged until tonsils were removed. No trouble since then. No worms.

*Present Illness.*—Seemingly normal baby in every way. Patient born three months after death of father and mother had to go to work and not able to give him the attention he needed; thinks he may have talked if he had been taught sooner. Said "daddy" at age of two years, but did not talk until four years of age. Weight only 7 pounds at birth. Had tonsils and adenoids removed by Dr. Lokey at four years, and soon after this began

Fig. 192.—A case of dystrophia adiposogenitalis.

to gain weight and is especially fat around the waist. When weighed here in office weight is 96 pounds. Height, 51½ inches. Patient nervous and restless. Squints and blinks eyes frequently. Stammers ever since he began to talk. Got zero in everything in school. Cannot promote him. Knows his letters pretty well.

Mother says patient was shriveled looking from three months to four years of age. Mother did not have enough milk

for him. Had a rash day after birth, probably from heat, and it passed off next day. Mother looks abnormally fat. Very happy natured child. Mother had a jar running for and jumping on moving train three months before his birth, and had pains that night and thought she was in labor, but the pains passed off. Patient's eyes did not focus well up to four years, and not very well since then. Does better in school work for past month, and quicker mentally and memory better. Very restless; can't be still or quiet; talks to himself much. No talking and only grunted before removal of tonsils and adenoids, but began to talk and talked about as he does now two weeks after operation. Very difficult for me to understand what he says, although his mother understands everything he says. Mother says she had never noticed absence of his testicles till I called attention to it, and penis seemed normal size till he began to fatten up and she thought the fat merely hid it.

*Neurologic Examination.*—Emotional state: Always been very nervous. Cries easily. Bad tempered, nervous, screams at times when he sees a dog or cat coming; afraid of animals. Excitable.

Psychomotor: Feeds himself; can dress himself. Headache when he gets hot. Sleeps well.

Mental: Always been backward mentally and physically. Went to school last year and this, and all marks were zero except in deportment and attendance. Forgets alphabet quickly. Can read a little. Can count a hundred, but cannot pronounce the numbers distinctly.

*Cranial Nerves.*—1. Perfume, R+L+; asafetida, R+L+; cloves, R+L+; mint, R+L+.

2. Normal.

3, 4, 6. Pupils equal; large. Light +. Accommodation +. No nystagmus. Muscles seem good.

5. Motor, normal. Sensory, normal.

7. Normal.

8. Seems good; co-operation poor for testing.

9. Nausea often. No dysphagia.

10. Vomits seldom.

11. Normal.

12. Normal movements. No tremor or atrophy.

*Taste.*—Rt. ant.: Acid +; sweet +; bitter +; salt +.

Lt. ant.: Acid +; sweet +; bitter +; salt +.

Rt. post.: Acid +; sweet +; bitter +; salt +.

Lt. post.: Acid +; sweet +; bitter +; salt +.

Speech: Very difficult to understand anything he says. Seems to understand what is said to him. Stammers.

Motor: Abnormal muscular movements, blinking of eyelids constantly.

Muscle strength: Easily fatigued.

Paralysis none.

Posture normal.

Tonus normal.

Co-ordination: Gait normal except feet a little far apart.

Romberg absent. Finger-nose normal. Finger-finger normal.

Trophic: Excessive weight for age and height.

Reflexes, deep: Rt. biceps +; triceps +; radial +; ulnar +; patel. +; Achil. +.

Left biceps +; triceps +; radial +; ulnar +; patel. +; Achil. +.

Reflexes, superficial: Rt. up. ab. +; l. ab. +; crem. 0; plan. +; Babin. 0.

Lt. up. ab. +; l. ab. +; crem. 0; plan. +; Babin. 0.

Cavernous reflex absent.

Sensation: Touch +; pain +; tem. +.

Nutrition: Weight 96 pounds. Height $51\frac{1}{2}$ inches.

Vesical functions: Wets bed every night and wet clothes often till a month ago.

Rectal functions: Did not control bowels till two months ago.

Fever 99.2° F.

Head mesocephalic; prominence of left cerebellar region; turns red when he gets hot.

Ears: Frequent earache and discharge since one year of age; better since tonsils were removed.

Teeth far apart; central incisors very large; lateral incisors absent.

Lungs negative. No cough, no blood, no sputum, no pain in chest, no night-sweats.

Dyspnea on exercising.

Heart: Examination murmur over whole body of heart systolic in time; not transmitted beyond heart. Pulse 25 during one-quarter minute. Blood-vessels normal. Blood-pressure 110/78. No varicose veins.

Abdomen: No hernia. Liver, spleen, and kidneys not palpable.

Appetite too good. Does not taste food. Nausea often. Vomiting seldom. No heartburn.

Intestines: No flatulence, mucus, diarrhea, blood, or piles.

Not constipated.

Rectum: Good control.

Genitalia: Penis measures 2.2 cm.; practically only head of penis shows. Both testes absent. No scrotal bag and appearance of groove in the center looking like labia, but closed up.

Urinary: No dysuria or hematuria. Diuria three to four times. Nocturia—wets bed.

Bones: Joints normal. Spine normal.

*Laboratory.*—Urine amber, clear. Sp. gr. 1.020. Acid 10 to 25 c.c. Albumin trace. Sugar negative, indican 4. Microscopically negative.

Blood: Hb. 75 per cent. R. B. C. 5,320,000. Leu. 6600.

Wassermann negative.

*x*-Ray by Dr. J. J. Clark. Complete examination of skull.

"Sella: Practically normal in size. There is a suggestion of slight posterior displacement of the posterior clinoidal processes. No evidence of intracranial pressure. Dentition progressing normally. There is evidence of a low-grade left antral infection. Frontals and ethmoids normal."

Report of Dr. Lokey:

"Removed tonsils in 1922. Fontanels closed after three years of age. Nose stopped up. Troubled breathing. Frequent styes. Otitis media. Conjunctivitis. Adenoids removed.

Small postnasal space. Left antrum cloudy. Fundi negative. Vision 20/20 without glasses and 20/15 with glasses."

Blood chemistry:

| | Mg. per 100 c.c. of blood. |
|---|---|
| Sugar | 100.0 |
| Non-protein nitrogen | 21.3 |
| Urea nitrogen (estimated) | 15.0 |
| Creatinin | 1.5 |
| Chlorids | 379.5 |
| Calcium | 14.0 |

Spinal fluid:

| | |
|---|---|
| Cell count | 5 per cu. mm. |
| Globulin | Negative |
| Sugar | Negative |
| Wassermann | Negative |
| Basal metabolic test | (—20) |
| Blood-sugar | 133.3 mg. per 100 c.c. blood |

Attempts to get carbohydrate tolerance test failed because patient vomited each time it was attempted.

Six weeks later carbohydrate tolerance test shows:

| | Mg. per 100 c.c. of blood. |
|---|---|
| Blood-sugar before glucose | 95 |
| ½ hour after | 143 |
| 1 hour after | 87 |
| 2 hours after | 100 |
| 3 hours after | 87 |

During the following two years the patient improved very much in his general condition, and practically ceased wetting the bed, and his habit spasm disappeared. He continued to gain in weight, however, and reached 131¼ pounds twenty-three months after the first note at the age of ten years and two months.

His mother was quite certain that before his operation—having his tonsils and adenoids removed—he was skinny and underweight, and immediately after the operation he began to gain weight rapidly, and finally reached a very abnormal weight for his age. I think it probable that in the removal of his adenoids a pharyngeal pituitary body was also removed and that this produced his dyscrasia.

The nurse whom he had in his early childhood was certain that his testes were normal, and when seen at age of eight years and three months they were not evident even in the inguinal rings, and seem to have disappeared entirely. He has erections, however, with a full bladder at night, and on examination. Only the head of the penis shows ordinarily. The patient was not normal before the operation, and it is difficult to say what his development would have been without the adenoid operation, but the time of becoming so fat is very suggestive of a pharyngeal pituitary body's having been removed.

## CLINIC OF DR. C. SIDNEY BURWELL

NASHVILLE, TENN.

### THREE TYPES OF CIRCULATORY FAILURE

SOME years ago White and Myers[1] suggested a useful method of classifying cases of heart disease, emphasizing the necessity of looking at every such patient from the points of view of the underlying etiology, the morphologic change present, and the resulting functional condition of the heart. In considering the functional condition of the heart the presence and degree of circulatory failure are of first importance. Circulatory failure is not associated with any constant morphologic change in the heart. It is recognized by changes in the circulation in parts of the body other than the heart itself. These changes may be objective, such as edema, or the condition may be recognized only by its effects on the comfort or activity of the patient. There is at present no very clear understanding of the precise nature of the alterations in the dynamics of the heart which underlie the signs and symptoms of heart-failure. It is not even known whether the same primary disturbance of function is present in all cases. The cases to be discussed illustrate certain variations in the manifestations of circulatory failure, and suggest corresponding variations in its mechanism and in its treatment.

**Case I.**—The first patient to be discussed is a stationary engineer thirty-seven years old. He entered the hospital complaining that he tired on slight exertion. He dated the beginning of his trouble to early youth, when he noticed that he could not exert himself as much as other boys without becoming short of breath. Twenty years ago he attempted to enlist in the navy, but was refused because of "heart trouble." This inability to exert himself without shortness of breath and palpitation kept him from doing various kinds of work in which he was interested, and gave many people the impression that he was lazy.

Seven years ago he found that vigorous exertion would bring on not only shortness of breath but also cough, sometimes with hemoptysis. This

combination has recurred several times since, always after severe muscular effort, and has always cleared up in a few days.

In childhood the patient had mumps, whooping-cough, measles, malaria, and pneumonia. There were frequent attacks of tonsillitis until 1919 when his tonsils were removed. He has been married for five years, his wife is well and has had two healthy children. The patient used a moderate number of cigarettes and drank coffee daily.

On examination the patient was a young man lying quietly without dyspnea or orthopnea. There was a decided malar flush, the fingers were not clubbed, and there was no fever.

The cardiac dullness extended 4 cm. to the right and 10 cm. to the left. The apex-beat was localized and tapping and was preceded by a definite short thrill. The rhythm was regular and the rate 70. On auscultation there was a loud snapping first sound preceded by a long rumbling diastolic murmur with a presystolic crescendo. No systolic murmur was heard at the apex and no murmurs were heard at the base. The pulmonic second sound was loud and ringing.

There were no evidence of peripheral congestion in the neck veins, no râles in the lungs, and no edema anywhere. The liver and spleen were not enlarged. Change in position caused a marked acceleration of the heart rate.

There were no abnormalities in urine or blood. The electrocardiogram showed large P waves and a right ventricular preponderance.

This patient had the classical signs of a severe grade of mitral stenosis. His symptoms are of interest in that they date far back into his youth and that in general, they are precisely the symptoms brought on in a healthy man by vigorous exertion. Their significance consists in the fact that shortness of breath (which is the chief symptom) occurs after much less exertion than is required to produce it in even a moderately healthy man. Now the conception of a "cardiac reserve" is a familiar one. It implies that in response to a need for a greater oxygen supply, such as exists during exercise, the normal heart can increase the amount of blood it pumps to the tissues to several times the amount needed by a resting body. But every heart has its limit, and when that limit is reached the owner of the heart will suffer from shortness of breath. Thus the amount of blood the heart can pump per minute is one of the factors which determine the degree of muscular exertion possible for a given individual.

This patient has an extremely limited exercise tolerance; he has only a small cardiac reserve. This limitation is apparently

due to the extreme narrowing of his mitral valve, through which only a limited amount of blood can pass per minute even under the high pressure which undoubtedly exists in the left auricle. The fact that he developed pulmonary edema and hemoptysis after exercise suggests that under these conditions his strong and hypertrophied right ventricle pumps blood into the lungs faster than it can escape through the narrow mitral orifice, leading eventually to such overdistention of the pulmonary vessels that fluid passes from them into the alveoli.

Digitalis cannot be expected to help this patient much. His difficulty is a mechanical one; his wisest course is to limit the demands on his heart to those which it can meet with ease. His life should be calm and his work sedentary. His heart has supported an abnormal load for years; he may be able to continue at light work for some time, particularly if he can avoid further damage to his heart by infection. To this end he is advised to treat even slight respiratory infection by rest in bed.

This patient illustrates a type of heart-failure characterized by inability of the heart to increase its output sufficiently to meet the metabolic demands of the body during ordinary activity.

**Case II.**—The second patient was on the surgical service and was seen in consultation. He was a man sixty years old who entered the hospital with a history of intermittent urinary difficulties for ten years and a recent history of sudden retention of urine.

On examination he was found to have a marked enlargement of his prostate gland with obstruction to the urethra. He also had certain cardiac signs of interest and with these we are more particularly concerned. The patient had been told several times before admission that his heart was very rapid and remembered several periods in the past when a period of rapid heart beat was associated with weakness and malaise. Examination after admission to the hospital revealed a rate of 160 per minute, which was practically unchanged by variations in position or activity.

The patient was a well-preserved old man with definite pallor and slight cyanosis of the lips and finger-tips. He complained of weakness and of slight shortness of breath. The neck veins were distended and no venous pulsations were visible. There was no edema. The cardiac dullness extended 4 cm. to the right and 11.5 cm. to the left. Auscultation revealed a rapid tick-tack rhythm and no murmurs. The blood-pressure was 94/74.

The lungs showed emphysema but no evidence of congestion. The liver was not enlarged. There was moderate sclerosis of peripheral arteries. The

electrocardiogram showed an auricular rate of 300 and a ventricular rate of 150, with the characteristic curve of auricular flutter.

The patient was given 1.6 gm. of digitalis in three days. There were periods of complete irregularity of the pulse on the second and third days. These were shown by the electrocardiogram to be due to an irregular block and not to any change in the auricular mechanism. On the fifth day there was an abrupt change to a normal sinus rhythm with a rate of 75. The patient was conscious of the change of rhythm, and immediately felt a sense of relief, of comfort, and of increased strength. The dyspnea disappeared after the change in rhythm and rate; the blood-pressure was then found to be 120/72.

In this patient we have an old man with some arteriosclerosis and a profound disturbance of the rhythm of the heart, leading to a constant rate of about twice the normal. The reversion of the rhythm to normal which was accomplished by the administration of digitalis and which was accompanied by a decrease in rate, resulted in prompt relief from the weakness and shortness of breath from which he suffered. His color also improved, and the pulse pressure more than doubled, as may be seen in Fig. 193.

The low blood-pressure, the cyanosis, and the weakness suggest that during the period of abnormal rhythm this patient was in a condition akin to surgical shock. In this condition the amount of blood put out by the heart has been shown experimentally to be diminished. The assumption of decreased output, as well as decreased blood-pressure, explains his symptoms satisfactorily as being due to an actual diminution in the oxygen supply to the tissues. They are symptoms of oxygen lack. It is important to note that digitalis was given to change the rhythm responsible for the failure and not to treat the failure itself, because in the shock type of failure digitalis probably does harm rather than good. As is usual in the type of circulatory failure exemplified by this patient he showed no edema of either lungs or periphery.

**Case III.**—The third patient was a colored woman forty years old, who entered the hospital complaining of attacks of a smothering sensation at night. She dated the onset of the symptom to about a year before admission when she noticed that after she had been in bed for an hour or two she would often awake feeling short of breath. This was relieved promptly by sitting up in bed. Later she began to have the same discomfort after eating a large meal or walking briskly up stairs. With these attacks there were sometimes cough and frothy sputum.

Before the onset of this trouble the patient had had excellent general health. The only severe illness was influenza in 1918, and there were no symptoms suggestive of cardiorespiratory, gastro-intestinal, genito-urinary, or neuromuscular disease.

On examination the patient was a well-developed colored woman, not acutely ill, but a little short of breath when lying flat. There was slight pallor of the mucous membranes. The pupils reacted normally but the

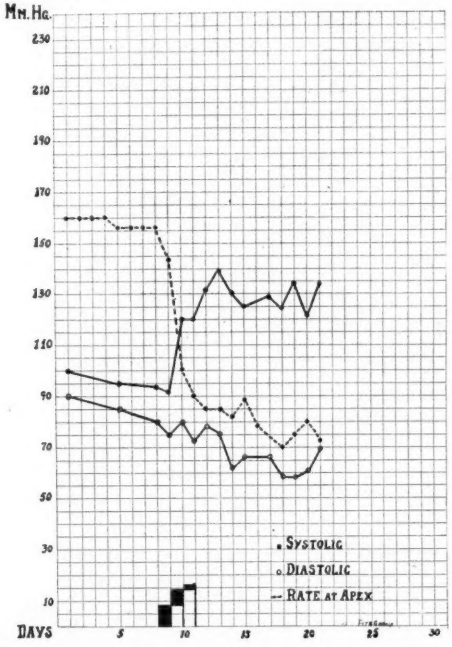


Fig. 193.—The relation of the heart rate to the blood-pressure. The shaded columns indicate amount of digitalis, in decigrams, administered each day.

fundi showed tortuous arteries, patches of silvery exudate, and flame-shaped hemorrhages. The radial arteries were thickened and irregular and the brachials were tortuous. The neck veins were not distended. The cardiac dullness extended 6 cm. to the right and 14 cm. to the left. The apex rate was 90 and the rhythm regular. A presystolic gallop rhythm was heard at the lower end of the sternum. There was a soft systolic murmur at the apex. The blood-pressure was 270/155.

The lungs expanded only fairly well but there were no râles or abnormal breath sounds. The liver was not enlarged and the abdomen contained no evidence of fluid. The urine had a specific gravity of 1.015 and contained

albumin and many granular and hyaline casts. The blood contained 3,900,000 red cells, 8000 leukocytes, and 60 per cent. hemoglobin by the Sahli method. There were 36 mg. of non-protein nitrogen per 100 c.c. of blood. The $CO_2$ combining power of the blood was 68 volumes per cent. The phenolsulphonephthalein excretion was 40 per cent. in two hours. The Wassermann reaction was negative.

After eight days of rest in bed the patient's blood-pressure was 240/135. At the end of this period at 9:15 one evening she had an attack of severe dyspnea during which she sat up in bed, breathed rapidly, and was in great distress. She coughed frequently, raising small amounts of foamy sputum. Examination of the chest showed many râles varying from fine moist ones to sonorous ones and most numerous over the lower lobes. Shortly after the administration of 15 mg. of morphin sulphate the paroxysm was relieved.

We see in this patient the victim of severe vascular disease, and very marked hypertension. The first and chief symptom of her heart-failure is paroxysmal pulmonary edema, usually occurring either at night or after exertion. The blood-pressure was not further elevated during the attack in this patient, but a study of a series of similar cases reveals that it is often higher than usual. In this case it may have been elevated above its usual height just prior to the attack. The paroxysm passed off after the administration of morphin. There is no evidence in the blood-pressure, the full pulse, the color, and the warm extremities of these patients, of any diminution of cardiac output, nor is it easy to see why a diminution of output should lead to a rapid accumulation of edema in the lungs only.

It is necessary here to introduce another factor into our discussion of heart-failure. It is obvious that to maintain normal circulatory mechanics there should be perfect co-ordination between the right and left ventricles, and that the two ventricles should expel exactly the same amount of blood with each beat, otherwise blood would rapidly accumulate either in the lungs, if the right ventricle puts out more than the left, or in the systemic circulation if the opposite condition holds. Normally the co-operation is perfect, each ventricle adapts itself instantly to receive and dispose of the amount of blood sent to it by the other. When the heart is damaged, however, especially when the damage is more extensive in one ventricle or when an excessive load is imposed on one ventricle, it is to be expected that the ability

of the chambers of the heart to adjust their work rapidly to changing demands may be diminished. Furthermore, it was shown by Welch,[2] in 1878, that mechanical interference with the action of the left ventricle could produce a change in its activity relative to the right ventricle and lead to pulmonary edema.

The history of this case suggests that the left ventricle, already supporting an enormous pressure, either received a call for increased work to which it was unble to respond, or that it failed to maintain its usual state of activity; that the right ventricle was able to increase or maintain its output temporarily, and that congestion and edema of the lungs followed. Morphin, by inducing quiet and perhaps by reducing the cardiac output, permitted the re-establishment of the normal distribution of blood. Morphin is the drug of choice in treating this paroxysmal type of pulmonary edema. It should not be combined with atropin, which may do harm by causing an increase in the heart-rate. Digitalis is not of assistance in combating an individual paroxysm, but in adequate dosage often diminishes the frequency of the attacks.

These 3 patients were selected for discussion because each of them serves to illustrate one of the disturbances of circulatory dynamics which may produce evidences of circulatory failure. Not many cases can be so readily explained, either because more than one factor is involved, or because unknown factors are at work, but in any case of circulatory failure, it is of interest to consider the possible mechanisms. Moreover, such an analysis is helpful in determining the best course to pursue in the management and drug therapy of the individual patient.

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# THE INTERPRETATION OF CHANGES IN BODY WEIGHT*

THE patient chosen to illustrate certain mechanisms of changes in body weight was a colored woman aged thirty-six years. She entered the Vanderbilt University Hospital on January 19, 1927, complaining of shortness of breath and nervousness.

**Present Illness.**—She dated the onset of her ill-health to between three and four years before her entry into the hospital, when she noticed that she was nervous and began to be sensible of a rapid heart-beat. At that time she weighed about 225 pounds, her usual figure, but in spite of an appetite that increased rather than decreased she began to lose weight.

About three years before admission she began to suffer from attacks of shortness of breath associated with exertion. These occurred at irregular intervals and she was often free of them for months. Two years before admission she began to have occasional swelling of her ankles, particularly toward night.

A year before admission she weighed about 175 pounds which represented a loss of 50 pounds in less than three years. During the year her disabilities increased steadily. Her shortness of breath increased, and was worse when she lay down, the swelling extended from her feet to her legs and did not disappear at night, her strength diminished, and her hands were unsteady. Seven intravenous injections "for her blood" gave her no subjective improvement. Her appetite continued to be good until three weeks before she entered the hospital. At that time she developed a cough, slight nausea, and frequency of urination.

**Past History.**—Her health as a rule was excellent. She was ordinarily a fat, strong woman, never ill except that she had many severe attacks of sore throat associated with fever and prostration. No other acute infections were recorded, nor any symptoms involving the gastro-intestinal, cardiorespiratory, genito-urinary or neuromuscular systems.

She had been married sixteen years and had had one pregnancy which resulted in a miscarriage at six months.

**Physical Examination.**—The patient was a large colored woman, obviously acutely ill and extremely short of breath. There was marked pitting edema involving legs, thighs, back, abdominal and thoracic walls, arms, hands, face, and eyelids. Not only were the eyelids swollen but the eyeballs themselves protruded. Aside from pallor of the mucous membranes the head showed no other abnormalities.

The thyroid was enlarged, a smooth bilateral enlargement without thrill or bruit. The neck veins were distended when the patient was sitting erect.

The chest expanded fairly well. There were no areas of dullness and no

* This case was presented to the second year class of the Vanderbilt University School of Medicine as one of a series of demonstrations of major symptoms.

changes in voice or breath sounds, but a few scattered râles at the bases of both lungs.

The area of cardiac dullness extended 12 cm. to the left and 6 cm. to the right of the midsternal line. The supracardiac dullness was 7 cm. in diameter. The heart rate was extremely rapid and the rhythm totally irregular. The rate at the apex was 180, and at the radial 100, a pulse deficit of 80. The first sound at the apex had a snapping quality, but no murmurs were heard at any area. The blood-pressure (taking the beats of maximum pressure) was 140/90.

The abdominal wall was edematous, but it was still possible to palpate a smooth, slightly tender liver edge 6 cm. below the costal margin. There was shifting dullness in the flanks and an easily demonstrable fluid wave.

The skin of the legs was tense and glossy. There was a slight, fine tremor of the extended fingers.

The urine had a specific gravity of 1.018, and contained albumin but no sugar. The sediment contained a few white blood-cells and no casts.

The blood contained 3,700,000 red blood-cells and 10,800 white blood-cells (79 per cent. of which were polymorphonuclears) per cubic millimeter, and 70 per cent. of the expected hemoglobin. The Wassermann and Kahn reactions were strongly positive. The non-protein nitrogen was 25 mg. per 100 c.c. The phenolsulphonephthalein excretion was 45 per cent. in two hours.

The electrocardiogram showed a ventricular rate of 180. There were no regularly spaced P waves, but many irregular fibrillary waves.

A teleoroentgenogram of the heart showed an arch 7 cm. in diameter. The left border of the heart was 11.5 cm. and the right border 6.5 cm. from the midline.

The patient was put at absolute rest in bed, the daily intake of fluids was limited to 1200 c.c., and the administration of digitalis was begun. In the first twenty-four hours she received 1.2 gm. of digitalis leaf. At the end of this period, the apical rate had fallen to 130 and the patient was much more comfortable. She received on the second day 0.6 gm. of digitalis leaf, and the same amount on the third day. When 2.4 gms. had been given in three days the apical rate was 90, there was no pulse deficit, and the patient's weight had fallen from 216 to 190 pounds. She was then placed on a daily dose of digitalis of 0.1 gm.

On the sixth day after admission, with pulse 90, the basal metabolic rate was determined and found to be 69 per cent. above the calculated normal. This was repeated three days later, and was 63 per cent. above normal. At this time the patient weighed 175 pounds.

After nineteen days of rest and digitalis the patient's weight had fallen to 138 pounds, a loss of 77 pounds. The heart rate at this time remained between 80 and 90 per minute, but was still completely irregular. On February 6th, for the first time, a rumbling, mid-diastolic murmur was heard just inside the apex. It began a short interval after the second sound, and varied in intensity from beat to beat. The pulse was not collapsing and there was no evidence of pericardial adhesions. Shortly before this time the administration of Lugol's solution, 0.3 c.c. three times daily, was begun. This resulted in very little change in the basal metabolic rate or the general condition, and on February 16th a partial thyroidectomy was performed under local anesthesia. The gland was found enlarged and showed definite hyperplasia.

Five days after the operation the basal metabolic rate was +45 per cent., a week later it was +23 per cent., and the patient was obviously much improved. She was less nervous and able to be out of bed without distress. At this time she began to gain weight, and a month after her operation, as may be seen from Fig. 194, she had gained 25 pounds with no signs of the reaccumulation of edema.

On March 8th the basal metabolic rate was +10 per cent. Since the reduction in metabolic rate had taken place without the re-establishment of normal cardiac mechanism it was decided to attempt the abolition of the auricular fibrillation by means of quinidin. Accordingly the administration of digitalis was stopped and that of quinidin was begun. Two small doses were given to test possible sensitivity of the patient to the drug. No toxic effects were observed, whereupon 2 gm. of quinidin sulphate per day were administered for four days. After 4 gm. were given the mechanism changed to auricular flutter with an auricular rate of 216 and a ventricular rate of 54, a so-called four to one response. Quinidin was continued for two more days and then withdrawn. The auricular flutter persisted after the withdrawal of the quinidin, and to combat it the administration of digitalis was recommenced; 1.3 gm. were given in five days, and at the end of that time the sinus rhythm was re-established with a rate of 65 and a

partial heart-block. Digitalis was withdrawn and the partial heart-block disappeared in a few days.

At this time the patient felt entirely well. She had no shortness of breath and was free of palpitation for the first time in years. Her weight at this time was approximately 25 pounds above the low point. She was discharged from the hospital ward to the syphilis clinic where she began a thorough course of anti-syphilitic treatment.

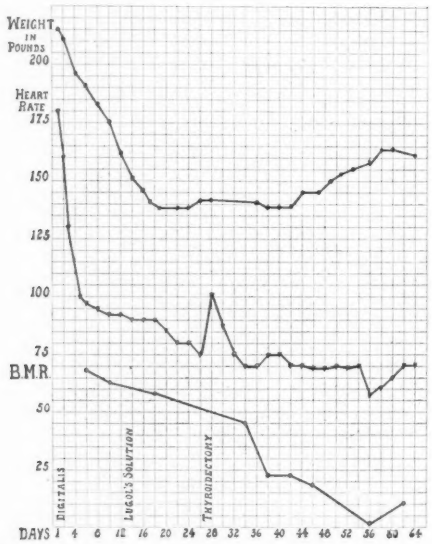


Fig. 194.—The weight of the patient during her stay in the hospital, charted against heart rate and basal metabolic rate.

She was last seen in July, 1928. At that time she considered herself well, was doing her housework without breathlessness, nervousness, or fatigue, showed no edema and weighed 203 pounds.

**Discussion.**—When the patient entered the hospital it was clear that she was suffering from severe congestive heart-failure and fibrillation of the auricles. This distribution of the edema was of interest in that it involved practically all portions of the

body supplied by the systemic circulation and tended to spare the lungs which are supplied by the lesser circulation. This is the distribution frequently seen in types of heart disease in which an excessive load is imposed upon the right ventricle. The complete etiology of the cardiac failure was not at first certain. The patient was suffering from thyrotoxicosis, and congestive heart-failure with auricular fibrillation is not rare in this condition, but her symptoms of heart-failure had developed rather early in relation to the symptoms referred to the thyroid disease. The marital history and the persistently positive Wassermann and Kahn reactions in the blood made syphilis a possible factor in the condition of the heart. Cardiac failure due to syphilis, however, is rare in the absence of aortic regurgitation, and it is extremely unusual to have auricular fibrillation associated with syphilitic heart disease. The low-pitched mid-diastolic murmur which became audible when the heart rate approached 90 was interpreted as being due to mitral stenosis which was probably the result of a previous endocarditis of the rheumatic type. This lesion (and the muscular damage presumably associated with it) plus the strain of the increased cardiac work caused by thyrotoxicosis were thought to be responsible for the early failure of the heart.

The need of the immediate situation was treatment of the cardiac failure. The administration of digitalis was followed by a striking reduction of the heart rate and a profuse diuresis with the rapid loss of 77 pounds of edema. When the edema had disappeared, an accurate estimation of the loss of body substance was possible for the first time.

The administration of Lugol's solution resulted in only slight improvement, and four weeks after admission a partial thyroidectomy was performed. A goiter of the hyperplastic type was removed and its removal was followed by a fall in the basal metabolic rate and a gain in body weight not due to the accumulation of edema. Further treatment consisted in the abolition of the cardiac arhythmia by quinidin sulphate and the beginning of treatment directed against the latent syphilis which was present. The diagnosis therefore included: Thyrotoxicosis,

chronic endocarditis (probably rheumatic) with mitral stenosis, cardiac failure, auricular fibrillation, and syphilis.

The changes in weight which constitute for us this patient's chief interest are shown graphically in Figs. 194 and 195. Figure 194 shows the fluctuations in weight during the patient's stay in the hospital charted against the fluctuations in pulse rate and basal metabolic rate. The initial enormous drop in weight is seen to follow the control of the heart rate by digitalis and to occur before the major changes in the metabolic rate. The gain in weight, on the other hand, is seen to occur after the fall in metabolic rate induced by thyroidectomy. Figure 195 is an

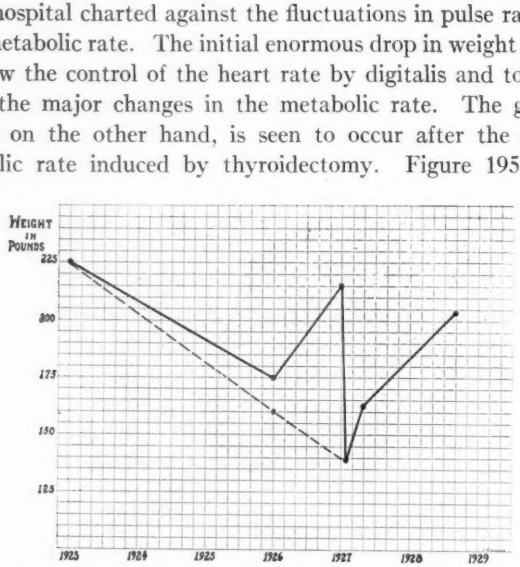


Fig. 195.—The variations in the weight of the patient over a period of five years.

attempt to indicate roughly the changes in weight since the beginning of the patient's illness four years before admission. It consists of two curves, one in which the actual body weights are charted, and a second, represented by the dotted line, in which the attempt is made to estimate the weight of the body without edema. In 1926, for example, a year before admission to the hospital the patient weighed 175 pounds. At this time she had some edema and since visible edema implies the presence of about 15 pounds of fluid at the least, that amount was subtracted from the gross weight. This procedure makes possible the construction of a weight curve the changes in which are due chiefly to the

thyrotoxicosis in addition to the curve combining the effects of thyroid disease and the variations in edema.

The variations in body weight in this patient are due to two main causes: First, a disproportion between the intake of food and the production of energy and, second, the accumulation or loss of fluid. These two mechanisms explain many of the changes in weight observed in patients. A brief analysis of these factors and certain others concerned with variations in body weight is warranted by the frequency with which these variations are met with in the study of patients.

In the first place the maintenance of a given weight implies an accurate balance between the food absorbed by the body and the energy produced. If the total daily energy production is increased by muscular exercise, fever, thyrotoxicosis, or even lack of sleep, and the intake of food is not correspondingly increased the patient will lose weight. This may be seen in people who exercise to reduce surplus weight, in patients (like the one described) with thyrotoxicosis, and in patients with tuberculosis or other long-continued fevers. Loss under these conditions may be prevented by adequate food, as may be seen in some thyrotoxic patients with very good appetites, or in patients with typhoid fever who receive a "high-caloric" diet. These last, if they receive sufficient food, may actually be heavier at the end of the disease than at the beginning.

Conversely if the total metabolism be reduced by rest, by a fall in temperature, or by disturbance of the controlling factors in thyroid or pituitary glands, and the food not correspondingly reduced, a gain in weight follows. This mechanism is illustrated by people who suddenly change from physical labor to sedentary occupations and continue to eat as much as before, by patients convalescing from fevers, and by patients with myxedema. The gain in weight associated with growth represents a positive food-energy ratio that is usually normal but occasionally, as when due to acromegaly, indicates disease.

Disturbances of the food-energy ratio due to variations in the amount of food intake are of many different types. People may and do overeat, and overeating often leads to overweight. On

the other hand many types of patients undereat. It is easy to see that people who cannot get enough food must suffer from starvation, and it is equally important to recognize that patients whose intake of food is reduced because of disease also suffer from starvation. Starvation in patients may be due to actual failure to ingest enough food, as in anorexia of all sorts, and in obstruction in the esophagus; it may be due to failure to absorb ingested food, as in persistent vomiting or constant diarrhea; or it may be due to disturbance of metabolism after the food is absorbed, as in diabetes mellitus.

In most cases more than one factor is operative. Thus in infections there is not only the elevated metabolism due to fever, but also the disturbance of appetite associated with the malaise. Similarly the loss of weight which is so important a sign of malignant disease may be due either to disturbances in digestion or absorption from the new growth itself, to reduction in the desire for food, or to increase in the metabolic rate.

The second group of causes of changes in weight has to do with variations in the amount of fluid in the body. Acute diarrhea may cause a loss of body fluid, but the usual way in which body fluid first alters body weight is by its accumulation in the body. Accumulation of fluid may occur as the edema of heart-failure or nephritis, as the ascites of portal obstruction, or as an exudate poured out in a serous cavity in response to some inflammatory change. This accumulation causes a gradual or sudden increase in weight. Removal of the edema by diuresis, tapping, or other procedure causes a converse change. Generalized edema, by its effects both upon the weight and upon the appearance of the patient, often masks a considerable loss of body tissue. Under these circumstances the loss of the edema will reveal an unexpected degree of emaciation. Most diseases which are capable of causing generalized edema can so interfere with the normal metabolic processes in the body as to cause also a loss of body substance. In a given case several factors may be present, some tending to increase and some to diminish the total weight of the body.

In addition to these more usual mechanisms of loss and gain,

one occasionally sees a tumor of sufficient size in itself to add appreciably to the weight of its owner. This is particularly true of cystic tumors of the ovary, but the occurrence of enormous cysts is now much less frequent than before the development of modern surgical methods.

With these general principles in mind we are prepared to interpret the weight curves of the patient. The initial loss is apparently due to the increased metabolism, with which her intake of food, in spite of an excellent appetite, failed completely to keep pace. As she developed heart-failure with edema it is probable that the basal metabolic rate still further increased; and according to her own story her appetite diminished. The loss of body tissue was thus accelerated, but its loss was obscured by the edema, and not demonstrable until a rapid diuresis carried away the accumulation of edema. Following the reduction in thyroid tissue effected by operation the metabolic rate fell to a level at which the ingested food was more than sufficient to maintain it and the body weight increased again almost to its original level. The fluctuations in this patient's weight are unusual in extent, but they serve the better for that reason to illustrate the mechanisms which must be considered in attempts to analyze the changes in body weight in other cases.

## CLINIC OF DR. C. L. ESHLEMAN

NEW ORLEANS, LA.

### SOME TYPES OF HYPERTENSION

I AM bringing before you today several cases showing abnormal blood-pressure findings. They represent different types of hypertension which are rather commonly seen in general practice, and I believe some interesting observations may be made regarding them.

I shall not pretend to enlighten you on the cause of hypertension. Numerous theories have been advanced, but after due consideration, we must finally acknowledge that we are nearly as much in the dark as ever concerning the fundamental causes underlying hypertension. That it is frequently, but by no means always, associated with nephritis and arteriosclerosis is well recognized; that it is commonly found with hyperthyroid states has likewise been noted, but many thyroid cases with thyrotoxicosis never show any abnormal blood-pressure elevations. That blood-pressure is sometimes raised to an abnormal extent seemingly in connection with infections and metabolic disorders, and during the menopause, and under the stress and strain of excitement, is a notable fact. Some of these conditions are well exemplified in these cases I shall show you today.

**Case I.**—This young white man of thirty was referred to me because two deaths from tuberculosis have occurred in his immediate family, and his employer has thought he looked tired and run down. He acknowledges fatigue and nervousness and loss of 5 to 6 pounds, but otherwise complains of nothing and attributes these symptoms to lack of rest and much worry over the recent illnesses in his family. In his history it is noted that six months ago he experienced transient dizziness on several occasions and on consulting his physician was told he had high blood-pressure. This statement somewhat surprised me because you will note that he is rather tall and slender, being actually 5 feet 11 inches and weighing only 128 pounds. He is asthenic looking, and of a type in whom tuberculosis is not uncommon, and in addition he was sent to me evidently with the question of tuberculosis in mind.

In this connection I might mention that tuberculosis and high blood-pressure are not common bed-fellows. In fact most tuberculosis cases have a low blood-pressure even in the early stages before debilitating effects of the disease have become prominent. One observer reports a group of 162 tuberculosis cases showing an average blood-pressure of 106/75, as compared with a control group of non-tuberculous individuals whose average blood-pressure was 120/80. Low pressure seems to be part of the strumous individual.

This man's appearance, therefore, suggested to me that he was of the type who had little energy and a poor supply of reserve strength, rather than the florid, energetic, driving type who so much more frequently show accelerated circulation and high blood-pressure. So, without prejudging him, I must confess that I would not have been surprised to find some early evidence of tuberculosis. His lungs were perfectly normal, however, and I was on the contrary somewhat surprised to find his blood-pressure 160/80 with a pulse rate of 100 per minute. On further examination I found no sign whatever of any organic disease. His circulatory system especially was free from definite signs of disease, the heart showed no enlargement, the palpable peripheral and retinal blood-vessels were not thickened or narrowed or tortuous. His urine was negative, the specific gravity showed normal ability to concentrate, he had no nocturia, denied headaches, and, in fact, had had no illness of any consequence in his lifetime.

While examining his heart, however, I was impressed by the fact that while it was perfectly normal in size, it was a little rapid and contracted with more force than usual, with changes of rate and force. I do not mean that the rhythm became intermittent, I mean that there was a change of rhythm rather of the sinus type. At times the rate would speed up and systoles were strong and loud, but in a few seconds would quiet down and assume a more nearly normal rate and force. This occurred from time to time, and I also began to notice fluctuations in his blood-pressure; at times it registered as high as 185/100 while a few minutes later it would drop 10 to 20 mm. both systolic and diastolic. At the same time the rate and force of his heart would diminish. He was manifestly a little nervous and showed fine tremor of his fingers. But you will note that his thyroid is not visible or palpably enlarged, and he does not impress one at all as a hyperthyroid case, and I might say also, that a recent basal metabolic observation was normal. He seemed relieved and anxious to be over with the examination.

This is undoubtedly a hypertension of nervous origin. After seeing him a number of times, when I took ample time to talk to him in a reassuring manner, I inspired confidence in him and explained to him that he had no real organic disease and that his blood-pressure was not a serious condition, but was merely elevated as a result of the nervous excitement while under examination. I did not hesitate to tell him that if I could in some way take his blood-pressure at night when he was soundly sleep-

ing and entirely oblivious of the fact that it was being taken that I felt sure that it would be perfectly normal. I am convinced that under full anesthesia he would show a normal blood-pressure, but while going under he would no doubt show a very marked but temporary elevation, especially of the systolic level. Men who give anesthetics tell me that this is a common occurrence in highly strung nervous persons.

Cases of this kind show temporary hypertension and are not uncommonly seen. They are quite frequently met with in examinations for life insurance, and it often requires considerable time and study to properly evaluate them as prospective risks. Many of them have already been rejected by a less careful and painstaking examiner, when a more searching study would have revealed the distinctly psychic character of the blood-pressure elevation. They are not really high blood-pressure cases, they are merely individuals who have a highly developed and sensitized nervous system, which responds in this manner to emotion or excitement. The particular stimulus may be anything which creates anxiety or fear; a visit to the dentist, a health examination, a visit to the operating room, the slight apprehension over an insurance examination with the lurking fear that some defect may be found, any of these things is sufficient to initiate this nervous syndrome, manifested chiefly by elevation of blood-pressure, and rapid pulse, and throbbing heart. It has not been sufficiently stressed that sometimes high blood-pressure is of this transient type. The conditions upon which it depends are not well understood. Temporary hyperthyroidism or hyperadrenalinism associated with or causing vasomotor changes might be suggested. Certain it is the condition is transient, not infrequently met with, and easily recognized if properly and carefully studied. I would call it a purely psychic transient emotional state without pathology, merely a functional response on the part of the circulation and blood-pressure to emotional stimuli in one whose vasomotor system is highly unstable.

After some further contact with this young man, which was largely reassuring and educational in nature, I found normal blood-pressure readings and he no longer manifested the other

nervous circulatory phenomena. I call attention to this type of case because in the milder forms it is often difficult to recognize at once as being a functional and transient condition, and many are made worse by being branded as high blood-pressure cases. A vicious circle ensues: their blood-pressure rises because of nervous causes, and their nervous equilibrium is further disturbed by the thought and fear of high blood-pressure.

**Case II.**—This next case is a lady who has been a patient of mine for ten years. She is now fifty-six years old. Her father died of apoplexy, her mother of heart trouble at fifty-six, one brother died of Bright's disease, one sister died suddenly in bed, four sisters are living and healthy, except one, who has high blood-pressure. Three brothers are living and healthy.

When I first saw her in 1918 she told me she had never been sick, she had not consulted a doctor in twenty-five years. Suddenly she had epistaxis which continued intermittently for a week. Her blood-pressure was found to be 200 at this time, dropping to 130 with the hemorrhages. She has been under my observation continuously ever since, and she is just as well today as she was ten years ago, except perhaps at times when nervousness and apprehension over her blood-pressure take hold of her and almost make her a nervous wreck. Her physical findings have varied little in ten years. She must have had a high blood-pressure for years before the epistaxis, because her heart showed left ventricular hypertrophy when first seen. She is neither stout nor thin, nor pale nor florid; her general appearance is of good health. Her eye-grounds show no findings of note, the vessels are neither tortuous nor sclerotic, her lungs and abdomen and skin and extremities are negative; all reflexes are normal. The temporal vessels do not stand out, the radials cannot be felt, and no definite evidence of arteriosclerosis can be detected anywhere. Her urinary output is not unduly large, the chemical and microscopic examination has always been normal, the phthalein excretion is normal, and blood chemistry is normal also. Her blood-pressure varies. The systolic is 160 to 190, the diastolic 90 to 110. She is her own barometer of blood-pressure. Occipital headaches of a throbbing character tell her at once when her blood-pressure is 20 or 30 mm. higher than usual. Epistaxis has not recurred, but uterine flooding spells have been rather frequent.

She has not aged a day in ten years as far as her physical examination is concerned. Only one thing has occurred, she has become increasingly apprehensive over herself. Unfortunately her husband was afflicted with arteriosclerosis, chronic nephritis, arteriosclerotic heart disease, and hypertension for years and died shortly after she discovered her own hypertension. The mental effect of this on her can be readily surmised. For years a similar ending has hung over her head. The death of any of her acquaintances from circulatory and cardiac accidents has further served to fan the flame of apprehension in her readily receptive imagination. And unfortunately she has read and acquired a smattering knowledge of blood-pressure from news-

paper and magazine articles, educationally directed, of course, but which I believe often create more anxiety than well-intentioned good.

This patient is a case of essential or idiopathic hypertension, a condition which is accepted by most clinicians as deserving of recognition entirely apart from the hypertension so frequently seen in connection with renal and arteriosclerotic disease. She has had a hypertension for at least fifteen years, but up to the present time has shown none of the renal or arteriosclerotic changes which frequently develop as a result of, or as associated features of hypertension. While she cannot be said to be a purely psychic functional type of hypertension like the first case there is certainly at times a large nervous element in her blood-pressure rises. A few years ago I was interested to observe her while going under the anesthetic for a herniotomy. Her blood-pressure rose to 220, but immediately dropped back to 160 while under full anesthesia. These psychic features cannot always be separated from the true effects of hypertension. They are a most difficult associated feature to be contended with. Too much reassurance renders them neglectful of certain restrictions advisable in their diet and mode of living, while too serious a view of their condition often makes nervous invalids of them, living a life of fear and dread, happy and encouraged when the blood-pressure instrument reads 160, but in a slough of despondency over 170.

Whether essential hypertension starts as nephritis or arteriosclerosis or ends eventually in one of these conditions, as long as it remains essential hypertension these patients deserve to have their treatment and prognosis tempered with judgment and not condemned, as many cases are, to a life of too great restrictions in diet and living which often puts them in the class of anxiety neuroses rather than hypertensive invalids.

**Case III.**—This third case is a lady of forty-two whose physician sent her to me three months ago. For three months previous she had had pains in her precordium, along the right side of the neck, and down her right arm to the elbow, especially on exertion and sometimes on lying down at night. She was dyspneic on exertion.

On examination at that time I noted that she was a short, stocky, slightly

florid woman who weighed 187 pounds, although her normal weight had been 205 pounds. Visible pulsation was noted in the carotids and episternal notch, her heart was enlarged, the apex being in the sixth interspace in the nipple line. Aortic dulness was slightly widened, a systolic murmur present at the base and a systolic at the apex of different intensity. Her pulse was regular, rate 104, blood-pressure 160/90. A short fat neck made palpation of her thyroid difficult and enlargement was recorded as doubtful. There was no tremor. The rest of her physical and laboratory examination was negative and she was considered a case of hypertensive heart disease with anginal symptoms. Because no definite evidence of renal or arteriosclerotic changes could be detected it was thought that her hypertension was of the essential type.

Treatment was advised and she was permitted to return to her home in the country. She returned a few days ago after three months, and you will see that she has developed other symptoms which at once indicate another diagnosis. She has not lost any more weight, but she is more nervous, looks frightened, has marked tremor of her hands, and at times you can note the distinct suggestion of exophthalmos; a characteristic staring expression and suggestion of sudden fright strike one at times. Her basal metabolic rate is only slightly elevated to +18, but the other symptoms are so striking that there remains no doubt that we are dealing with hyperthyroidism. Her blood-pressure for the past three days has been variable, one day it was 148/78, not abnormal except in the wide pulse range. Another time it was 170/90, pulse rate 122; other observations were 152/78 and 185/100. I find these fluctuations quite frequent in cases of hypertension due to hyperthyroidism and it seems to go hand in hand with the generally unstable state which these patients show. Their pulse rate, while always rapid, fluctuates sometimes within a wide range; attacks of auricular fibrillation come and go in some cases and variations in blood-pressure likewise occur. This is another disease which one should always keep in mind in connection with hypertension. I do not mean to say that all thyrotoxic cases show hypertension, but many of them do, and it should always be considered a possible cause and a careful study for other signs and symptoms of thyrotoxicosis should be made. This patient did not present a sufficiently definite group of symptoms to justify a diagnosis three months ago, but now there can be no doubt of it. She will of course have a thyroidectomy done shortly, or as soon as her condition justifies it.

**Case IV.**—This next case is a young woman of forty-two who was admitted to my service recently because of headaches, nausea, vomiting, high blood-pressure, and nervousness. She has had sick headaches for fifteen years. Now sick headaches in women usually mean migraine, about which little is known etiologically. There does not seem to be any connection with hypertension. Fifteen years ago this lady's blood-pressure was found to be too high and was connected with the headaches she has had at times ever since. During the past four years her headaches have been much more severe, sometimes frontal and sometimes occipital, and her vision has gradually become affected to such an extent that, at present, newspaper print appears

so blurred that she cannot read it at all even with the aid of her glasses. She has some nocturia and on several occasions recently she has had transient attacks in which she has been unable to speak and has felt numb in her right arm. Last week, the nurses tell me, she had an attack of this sort lasting about ten minutes, after which she was perfectly normal again. In the attack she seemed confused and unable to tell them what she wanted. She says she was conscious and knew what she wanted but could not speak; a rather typical transient aphasia.

You will note that she is a rather thin but not emaciated woman, who is not acutely ill. She is bright and answers questions readily and accurately. Her heart is markedly enlarged downward and outward, a rather loud systolic murmur heard at the apex and aortic second is much accentuated. Her radial vessels are distinctly palpable. Her blood-pressure 278/170. The eye department reports that "both eyes show optic neuritis, in the left eye papilledema; arteries are thin and sclerosed, the veins a bit full, vessels slightly tortuous and a few fine hemorrhages." The opinion is expressed that the condition is due to "kidney or vascular changes."

Her urine shows only an occasional trace of albumin and a few hyaline casts with an average specific gravity of 1.014 and a normal to slightly increased twenty-four-hour output. The phthalein excretion is 55 per cent. in two hours, and the blood chemistry shows total non-protein nitrogen 33.3, creatinin 1.25, uric acid 2, dextrose 76.

This is certainly the very worst type of hypertension. The outstanding feature of her case is arteriosclerosis, advanced in one of her age, forty-two, and associated with an unusually high blood-pressure, both systolic and diastolic. While her kidney function seems good and there is apparently no nitrogenous retention, I do not think one can doubt that she has arteriosclerotic renal changes. Her eye-grounds are in very bad condition and no doubt the cerebral vessels are extensively degenerated. Her prognosis is very bad and when eye-ground changes of this sort ensue they rarely go on longer than a year without some serious event occurring. First, an attack of apoplexy is not unlikely at any time; second, a cardiac break may occur with edema and death in that way; anginal attacks sometimes end such cases without decompensative phenomena; third, a renal death may be in store for her although the apparently satisfactory renal condition at present makes this seem least likely. These are the worst types of hypertension we meet with because they are built upon an arteriosclerotic foundation, or arteriosclerotic changes have developed and progressed gradually with them. This is an unalterable condition and one which is very intractable.

**Case V.**—This last case, whose history is before me, is somewhat similar to the one just shown you. He died recently. He was fifty-three years old and had had no severe illnesses. His brother, who is a physician, found hypertension and albuminuria a few years ago for which he had advised certain restrictions in diet and living. Three weeks ago he brought him to me because he had vomited several times the previous week without any apparent reason, and complained of failing vision.

On examination I found a fairly well-nourished and developed man with

marked general arteriosclerosis, blood-pressure 230/158, hypertrophied heart with reduplication of the first sound and accented aortic second. His urinary output was normal in amount, but showed a remarkable fixation of the specific gravity. The gravity of every specimen passed day and night for seventy-two hours was taken by the nurses. It was practically fixed at 1.010. The highest noted was 1.019 on one occasion, the lowest was 1.008. Practically all the others were 1.010. Albumin was present in large amount and much pus and a few hyaline casts. His phthalein output was 20 per cent. in two hours. The blood chemistry was normal except a uric acid of 6.4. Wassermann negative. His eye-grounds showed papillary edema. Two weeks later he showed clouding of consciousness, poor orientation, and restlessness. There was no edema anywhere. His phthalein output dropped to 5 per cent. in two hours and as he grew worse his blood chemistry showed slight elevation of the total non-protein nitrogen. After two weeks more he developed convulsions and died twenty-four hours later. This case was similar in character to the previous one except that the hypertension was associated with extensive renal changes and his death was due to uremic poisoning.

The types of hypertension illustrated by these cases are commonly seen. Many other cases might be cited but I believe these bring out most of the important points to be studied. The prognosis is often difficult, but where cardiac, vascular, and renal changes are not too advanced good judgment would seem to dictate that we do not take such a serious view of our hypertensive patients as to make nervous invalids of them in their efforts to carry out innumerable and unreasonable dietetic and living restrictions.

## CLINIC OF DR. BRYCE W. FONTAINE

MEMPHIS, TENN.

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# A CASE OF TROPICAL SPRUE ENDEMIC IN TENNESSEE. DIAGNOSIS AND TREATMENT

MY experience with tropical sprue has been limited to a few cases in teachers and missionaries, invalided home from Korea and the Philippines, presenting themselves for the purpose of having blood-counts made. Their bowel disturbances have usually subsided during the rest necessary in making the voyage home.

I am familiar with the splendid articles of Wood,[1] Simon,[2] Boyd,[3] Musser,[4] and others, reporting cases of sprue occurring in the Southern States. Each of these observers has called attention to the danger of its becoming endemic in the South.

I have had many cases of rather resistant diarrhea, lasting as long as six or eight weeks, and after excluding the possibility of an amebiasis, pellagra, or local conditions in the rectum, I have so far been able to class all of them as gastrogenous diarrheas, secondary to achlorhydria.

All of these cases have shown a complete lack of free hydrochloric acid in the gastric contents. In some the cure has been difficult, requiring weeks, but in the end all have yielded to large doses of dilute hydrochloric acid.

My personal experience has, heretofore, kept me from accepting unreservedly the claims of these pioneer investigators that sprue is not essentially a tropical disease, that it can occur in the Southern States in individuals who have not been to the tropics, nor have had any personal contact with others sick with the disease, or carriers, and that there is a possibility of its becoming endemic in the South.

Within the past few months a case has presented itself to me, which undoubtedly originated in Tennessee. I wish to report

this case, with remarks upon the diagnosis and treatment of the disease, but not without many misgivings, and due apologies to Wood, and others, who for many years have appealed to unsympathetic audiences and readers, making apparently futile efforts to impress upon the Southern physician the importance of this subject.

In my efforts to recognize and treat this troublesome condition, I have referred freely to the literature, and what I have to say comes very largely from the experience of others, as well as my own, in the study of this single case.

**Illustrative Case.**—Mrs. W. A. E. aged fifty-nine years. Married. Native of West Tennessee. Occupation housekeeping and renting of rooms. Consulted me because of following complaints: loss of weight and strength, a painless diarrhea, occurring at intervals for the last four or five years, often associated with a sore tongue. The attacks usually lasted for three or four days, the number of stools five or six, always occurring in the morning. They were absolutely painless and, so far as the patient can tell, never contained blood or mucus. The attacks lasted three or four days, and disappeared, returning in one or two weeks. In the beginning there was no great loss of weight or strength, and the patient's general health was otherwise good. For the past nine months, the diarrhea has become much more persistent, continuing almost constantly, until the present time. During this time she has lost weight and strength, and estimates that she has lost 50 pounds. She has never had any fever, but a sore tongue has been frequent. During the early development of the diarrhea, the stools retained their normal color, but recently have varied from gray to light brown, with a sour, nauseating smell. During the last six months there have been nausea and vomiting, occurring once or twice a week. Until coming under my observation, the patient's diet consisted principally of eggs, biscuit, butter, syrup, coffee, sugar, and cream for breakfast; vegetables, macaroni, bread, butter, pie, buttermilk for dinner; and for supper she usually ate the left overs from the midday meal. She has always been fond of fruit, vegetables, chicken, and fish. Four months ago, in the course of a routine examination by another physician, an analysis of her gastric contents was made, and she was told that she had an absence of free hydrochloric acid. Since then she has been on a strict diet, and has taken one teaspoonful of dilute hydrochloric acid in water three times a day, without any benefit. The previous health of this patient has been good. She never had a serious illness, except an attack of gall-stone colic thirteen years ago, necessitating the removal of the gall-bladder and stones. As a result of this surgery she obtained complete relief from the colic. She has had three children and one miscarriage. The menopause occurred at forty years. Patient has lived continuously in the region contiguous to her home in west Tennessee, except for one visit to Missouri about three years ago, and one visit to neighboring towns in Arkansas and

Cairo, Ill., two years ago. There is no record of her ever having been beyond a radius of 150 miles from her home during the last eighteen years, nor has she ever been in a tropical or a subtropical climate. So far as she knows, she has never come in contact with a person suffering from a complaint similar to hers.

The physical findings in this case reveal a middle-aged woman, poorly nourished, slightly paler than normal, skin normal in appearance, with no eruption on face, hands, or feet. The heart is entirely normal in area and the sounds are clear. The lungs show normal fremitus and resonance. Breath sounds are clear throughout, and there is a normal excursion over both bases. The abdomen shows a faint scar over the right hypochondrium in the region of the gall-bladder, resulting from the former surgical operation. The abdomen is scaphoid in appearance. There are no masses, no areas of rigidity, nor points of great tenderness. Blood-pressure is 120/68. Patient's weight is 115 pounds (her former weight was 165 to 175 pounds), her height is 5 feet 4 inches, her pulse rate 68, her temperature 98.4° F. Her throat is entirely normal; tonsils not hypertrophied nor infected. The tongue is slightly red and smooth. The patient is wearing upper and lower plates. Gums are slightly redder than normal. The joints are normal. There are no palpable or visible lymph-glands. Reflexes are active. The pupils react normally to light and accommodation. A proctoscope, 20 cm. long and 2 cm. in diameter, was passed into the bowel a distance of 18 cm. without difficulty. There are no hemorrhoids or evidences of an abrasion, ulcer, or tumor in the rectum. The mucous membrane of the rectum is intact throughout, but is much more reddened in appearance than normal. There are isolated deposits on the mucous membrane of the rectum, resembling patches of thrush, as seen on the mucous membrane of a child's mouth. These vary in size from a mustard seed to a pea, are gray or white in color, and can be scraped off without difficulty.

The electrocardiogram shows a normal rhythm and conduction in all three leads.

Roentgen-ray and fluoroscopic examinations show the lungs, heart, and aorta normal. The film made on the Bucky-Potter diaphragm is normal. The stomach is normal in outline with two peristaltic waves and a normal duodenal cap throughout. The barium enema shows a slightly redundant colon, the shadow being somewhat obscured by barium in the stomach and small intestine. No filling defect or other deformity is noted. The sinuses are clear.

A voided specimen of urine is amber in color, acid in reaction, with a specific gravity of 1.023, showing a faint trace of albumin, no sugar, but a trace of bile. There is no blood. The test for indican shows no increase. There is no acetone or diacetic acid. The centrifuged specimen has a very slight sediment, which under the microscope reveals a moderate number of epithelial cells from the lower genito-urinary tract, a few pus-cells, and an occasional hyaline and pale granular cast. In a study of the blood, the hemoglobin reading is 80 per cent. (Dare), the leukocytes 7700, erythrocytes 3,982,000, color index 1. There are no normoblasts, no megaloblasts, a moderate anisocytosis and moderate poikilocytosis, no polychromasia, and no para-

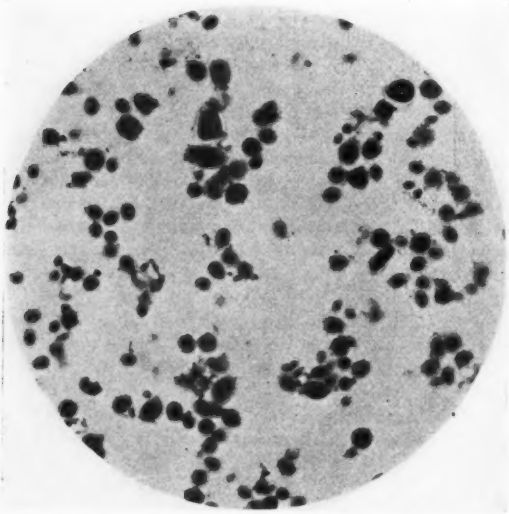

Fig. 196.—Photomicrograph of hanging-drop preparation from pure culture monilia, forty-eight hours old (×1200).

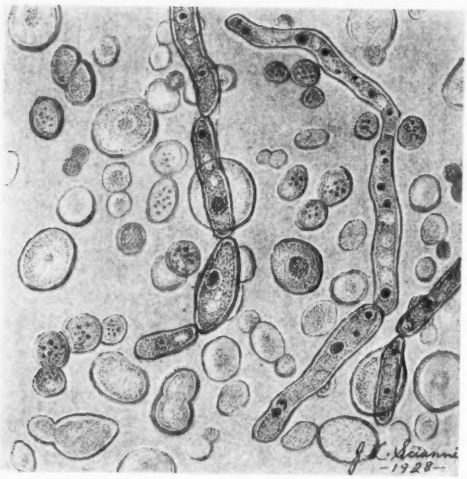

Fig. 197.—Composite drawing showing monilia in various phases of development—young yeast cells, single and budding, some large old cells, or dauerzellen, and two types of mycelia.

sites. The differential count is polymorphonuclears 55 per cent., lymphocytes 33, large mononuclears 8, eosinophils 2, mast-cells 0, myelocytes 0, transitionals 2. Blood Wassermann test is negative. Eighteen c.c. of the gastric contents, removed one hour after a Mayo test-meal, are normal in color and character, fairly well digested, contain no bile, but a faint trace of occult blood (probably caused by traumatism from the tube). The starch is fairly well digested. There is no free HCl, combined HCl 8, and total acidity 8, no organic acids, no lactic acid, and no albumin. Microscopic examination reveals a few starch granules, a few epithelial cells, mucus, and blood-cells.

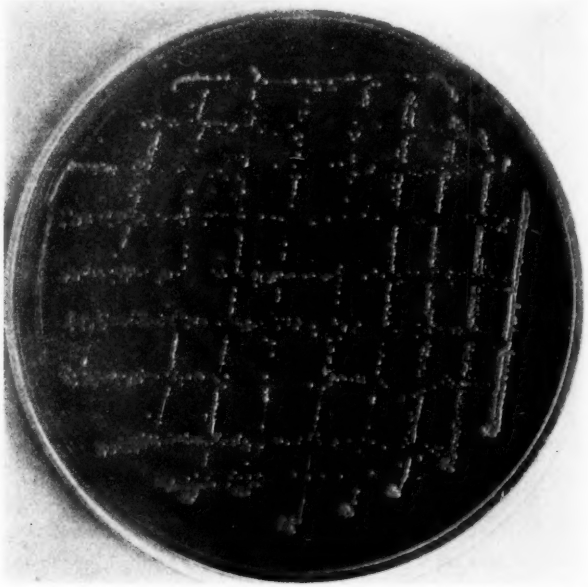

Fig. 198.—Plate of Sabouraud's medium showing colony characteristics of monilia six-day-old culture.

The stool is light yellow, or drab, in color, of the consistency of heavy cream—pultaceous (MacLean[6])—with a very offensive odor of decomposing acids. It is acid to litmus and phenolphthalein. There is no occult or visible blood. It contains particles of macroscopic fat, with a slight amount of mucus. Microscopic study shows numerous fatty acid crystals, fat globules, numerous yeast cells (some of which are budding), a few starch granules, a few epithelial cells, and numerous motile bacilli of the colon type. In a study of many mounts no ova, parasites, or cysts are seen. Slants of Sabouraud's medium were inoculated from the stool, and after three days' growth, plates

were made on the same medium, and cultures were submitted to the Department of Bacteriology of the University of Tennessee, from which the following report was submitted:

*Direct Examination.*—Hanging-drop preparations show a mixed culture consisting of a yeast and a bacillus. The yeast forms are round or oval (round forms predominate), 3 to 7 mm. in diameter, and reproduce by budding. They are bright and clear cut, appearing with a double contoured wall (Fig. 196). The nucleus is distinct, and a peculiar brownian-like movement of a bacillus-like body inside the yeast is noted. In addition to the round and oval forms there are elongated forms, with slightly rounded ends which suggest

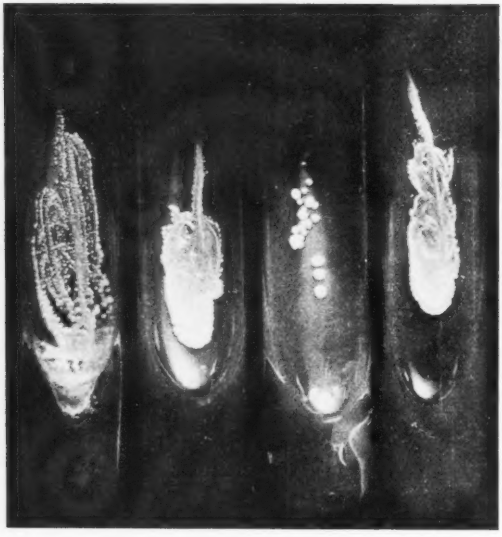

Fig. 199.—Six-day-old cultures of monilia on Sabouraud's medium, at room temperature.

sausages. In these usually three (sometimes two) distinct nuclei-like bodies are noted. Usually these elongated forms are isolated, but sometimes there are several (two or three) of them hanging together, forming a mycelium-like effect. A terminal round form is noted on some of these. There are various formations of the round types—pairs, short chains, and groups, with abundant bud production (Fig. 197). Smears were Gram stained and the yeast was found to be Gram-positive, the bacillus Gram-negative (evidently a member of the colon-typhoid-dysentery group).

*Isolation of Pure Culture.*—Pure cultures of the yeast were obtained by growing the mixed cultures in infusion broth to which was added lactic acid

1 : 50 and 1 : 100 (suggested by Tanner). After twenty-four hours subcultures were made on Sabouraud's medium, and these yielded only the yeast organisms. Hanging-drop preparations of these showed only typical yeast forms, no mycelia.

*Colonies.*—Petri's dishes containing Sabouraud's medium were streaked with these pure cultures (Fig. 198).

The colonies (after five days' growth at room temperature) are round and regular, 1 to 4 mm. in diameter. The growth is white and of creamy texture, shining, and heaped in the center (Fig. 199). Occasionally a dry, slightly rough, flat, "dirty white" effect is produced.

*Mass Growth.*—Growth on Sabouraud's and other solid media is luxuriant, smooth, and creamy, shining and easily picked up with the inoculation loop (Fig. 200). There is a characteristic sour, fruity odor (suggests over-ripe apples to me) about the cultures—not unpleasant odor. (Note: Dr. Campbell calls it a "sour honey" odor.)

*Cultural Reactions.*—The following cultural reactions were given by the yeast organism (all growth at room temperature):

| | | | |
|---|---|---|---|
| Dextrose | —Acid (slight) | Saccharose | —Negative |
| Maltose | —Acid and gas | Mannite | —Negative |
| Levulose | —Acid and gas | | |
| Galactose | —Acid | | |
| Lactose | —Negative | | |
| Arabinose | —Negative | | |
| Rabbinose | —Negative | | |
| Dextrin | —Negative | | |
| Inulin | —Negative | | |

Litmus milk—Initial slight acidity, followed by alkalinity, no coagulation
Indol —Negative
Plain broth —Broth clear, sediment
Gelatin —No liquefaction—growth around edge of tube—no mycelium produced

The fermentation results were the *same*, one day and ten days after inoculation.

*Further Observations.*—On July 21st the yeast culture was transplanted to a number of special media (types used by Dr. Michelson in his exhibit work). It is interesting to note that neither gentian-violet, acriflavin, nor bile exerts any appreciable inhibitory effect on the growth. Thymol had some inhibitory effect, but did not prevent growth as is the case with Dr. M.'s blastomycetes cultures.

On July 23d mycelium growth was noted on media 36, 38, 12, and old Sabouraud's slants. These are short feathery tufts extending down into the medium. Hanging-drop preparations from the cultures show very nice mycelial formations—short chains of the sausage-like forms, ending usually with a round form. Some peculiar forms were noted, too, which suggested the signet-ring effect described by Ashford.[6] These are evidently old yeast

cells. Other cultures marked "E. 6/29/28" and "E. 7/14/28," were received July 21st. These cultures were also mixed and pure strains of the yeast were obtained in the same way as described above. Morphologically, the yeast is the same in all three cultures. Identical cultural reactions were obtained with the three cultures. Morphologically, this is a form of monilia. The organism reproduces chiefly by budding in culture, though mycelial forms are noted in hanging-drop preparations and on certain media (Fig. 201). No asci are seen. Morphologically, it resembles Ashford's psilosis (or Castellani's Monilia Enterica), but the fermentation and gelatin reactions do not check with those given for this species. It cannot so far be placed in any

Fig. 200.—Ten-day-old cultures of monilia on Sabouraud's medium, at room temperature.

species given in the table of Castellani and Chalmers,[7] but the cultural and morphologic characteristics are, for the most part, suggestive of Monilia psilosis, and are of the subtype "C," which will conform to the work of Hannibal and Boyd,[8] in which types of monilia A, B, C have been found in sprue.

*Additional Notes.*—Mycelium very poorly developed, yeast form predominates in cultures. Usual type of growth on agar slants is smooth, creamy, shining. Gelatin stab—after twenty days—does not show inverted pine tree growth, nor liquefaction. Litmus milk (reaction checked) remained alkaline—no coagulation.

Clinically, the patient presents symptoms that are strongly suggestive of tropical sprue, viz., sore tongue, secondary anemia, a painless diarrhea

without visible blood in the stools, occurring without tenesmus, much worse in the morning, marked loss of weight and strength, no clinical evidence of tuberculosis in the lungs or bowels, syphilis, pellagra, amebic, or other parasitic infections in the bowel, bacillary dysentery, no chronic, inflammatory, or malignant disease in the rectum or pancreas.

This clinical picture alone is not of easy differentiation from that presented by patients with gastrogenous diarrhea or pellagra. In the absence of the skin manifestations, or the nervous symptoms of the latter, the chief means of differentiation is a

Fig. 201.—Photomicrograph of monilia stained with methylene blue, showing yeast stage and mycelia (×1000).

study of the stools by cultural and microscopic methods, in order to demonstrate yeasts, or any possible collateral infections by parasitic entozoa. In sprue the stool, gray to mustard yellow in color, has the appearance of heavy cream, an odor of rancid fat, sour apples, or sour honey, and shows fat macroscopically and microscopically, whereas the stools of pellagra and gastrogenous diarrhea show simply liquid undigested fecal matter, without any characteristic odor or color.

It is out of place in a contribution of this character to discuss at length the relation of yeasts to the etiology of sprue. However, it is impossible to discuss intelligently the diagnosis and treatment without a reference to some of the important facts already recognized and seemingly established by the students of the disease. Kohlbruggei,[9] in 1901, states that he found yeast cells in the scrapings from the tongue and esophagus. Following this Castellani, in 1905 and 1912, described several varieties of yeast found in this disease which he called Monilia intestinalis. This earlier work was again confirmed by Manson-Bahr,[10] in 1913, who found the same yeast cells in mucus from the mouth and tongue scrapings. Still later, in 1917, comes the report from Dold[11] in China, stating that he was able to grow yeasts in 7.5 per cent. of normal stools, in 16 per cent. of stools in patients with diarrhea, but not like that of sprue, and in 92.1 per cent. of the cases that were undoubtedly sprue. This same observer was able to produce a diarrhea closely resembling sprue by feeding cultures of yeast to white mice. This last experiment of Dold's was repeated in the case of guinea-pigs by Smith,[12] who produced sprue symptoms by feeding a diet deficient in vitamins, and subsequently introducing Monilia psilosis into the animals' stomachs.

In contradistinction to the observation of the last mentioned observers, Anderson[13] reports that most yeasts when fed to man, pass through the alimentary canal in a living condition, not even gaining a temporary foothold. Bovaird[14] in this country, in personal experience with cases brought to New York City, was able to find monilia in only 1 case out of 13 under observation. His report is open to criticism, as his study was limited to direct smears from the stool, without effort to culture the organism upon suitable media.

Ashford's work has been classical, and his experience in the number of treated cases is perhaps greater than any other living author. Therefore, his conclusion that yeasts, especially the variety Monilia psilosis, are the chief etiologic factors in sprue, occurring in 83.6 per cent. of the known cases, has the ring of authority, and must be given careful consideration, especially

since his work has been confirmed by such investigators as Wood,[15] Smith,[12] Rogers,[16] Bahr,[17] Oliver,[18] Michel,[19] and many others.

We cannot ignore the fact, however, that Castellani, the most able student of fungi and yeasts in the world, states that while yeasts of the variety of oïdia sometimes occur in the intestinal tract in sprue, they have nothing to do with its etiology, and the only part they play is in the production of frothiness of the stools. Castellani's idea of the lack of pathogenicity of the yeast, so far as sprue is concerned, has long been accepted by many other workers in tropical medicine. Only recently, in a personal communication from a very prominent investigator in the Public Health Service, I was given to understand that the theory concerning monilia as an etiologic factor in sprue, is very much on the wane. My experience is too limited to express an opinion, except to say that in cultural methods from the stools of other types of diarrhea, I have never encountered yeasts in any notable quantity.

While this case was under observation, there was in the same hospital a case of pellagra, with achlorhydria and severe diarrhea, from which efforts were made to grow yeasts from the stool on the identical culture medium, under the same conditions, and technic, with negative results. Despite the fact that Manson[20] insists that sprue is a disease *sui generis*, I have had to rely upon the demonstration of yeasts in the stools for my diagnosis. It was based largely upon my ability to grow repeatedly from the stools, yeasts corresponding in the main to the cultural characteristics of the Monilia psilosis. An attempt was made to carry out the complement-fixation test on the blood-serum with various strains of monilia, but lack of experience with the method prevented a satisfactory test, and it was given up. In a discussion of tropical sprue the clinical history of a painless chronic diarrhea, of the morning type, with stools of a characteristic color and odor, showing an absence of blood and mucus, but the persistent presence of a yeast conforming to the type of monilia, accompanied by anemia and loss of weight and strength, in the absence

of any other etiologic factor, should be sufficient evidence for a diagnosis.

The literature upon the treatment of sprue, as it occurs in the tropics, is so voluminous and varied, depending upon the authors' uncertain views as to the etiology of the condition, that it can hardly be fully discussed in anything short of a monograph. So much has been written on the subject, at such great variance, that one is almost inclined to believe there is no specific treatment, and that the disease, like amebiasis, is very difficult to cure; many patients never recovering. If all observers were in agreement that Monilia psilosis alone is the etiologic factor, the treatment could be attempted upon rational lines. Whether or not it is the sole etiologic factor, the fact must not be ignored that it is present in the intestinal tract in the majority of cases, and that most observers by proper cultural methods have been able to grow it in abundance from the stools. Ashford's work shows that it occurred in 83.7 per cent. of the cases, and Dold's, in China, in 92 per cent.

Accepting the undisputed fact that the yeasts are abundant in the intestinal tract, the first thing that would suggest itself in the treatment would be the administration of a vaccine, made from this same yeast, or the use of an intestinal antiseptic, harmless to the patient, which would inhibit, or totally destroy, the growth of the yeast in the intestinal tract. The first measure has been tried out with varying success. A report of the work of Michel[21] gives much promise, but even Ashford says, "While vaccines do some good, they will not alone cure, nor prevent relapses of the disease, and they must be prepared by experts to be of any value at all." The preparation of the vaccine is difficult, requiring one well-trained in the technic, and results are so uncertain that Ashford and Michel are practically alone in their endorsement of this therapeutic measure.

Many intestinal antiseptics have been suggested, and given trials—sulphurous acid, thymol, menthol, chlorin, and quinin, calomel, perchlorid of mercury, salol, acetozone, benzosol—all with limited effect in the cure of the disease. The use of yellow santonin was suggested by Colin,[40] in 1878, and later on

Begg[22] made a very thorough study of its value, even to the point of writing a monograph on the subject. He considered it almost a specific. The cure was supposed to have been brought about by ridding the intestinal tract of micro-organisms, perhaps entozoa —most likely the Strongyloides intestinalis. At this time no mention was made of the drug's probable inhibitive effect upon the growth of yeasts in the intestinal tract. In Begg's report there was some confusion of sprue with certain other tropical diseases, and doubtless he successfully treated, along with sprue, many other parasitic diseases causing diarrhea. In view of the favorable report of the use of santonin, it occurred to met that the drug might have some inhibition upon the growth of yeasts. Cultures were grown in various strengths of santonin, with the following results:

Yellow santonin, which has been aged by exposure to sun, of the formula $C_{15}H_8O_3$, anhydrid santonic acid. Practically insoluble in water, soluble in alcohol, 1 gm., 43 c.c. alcohol. Saturated solution (alcoholic) was made and added to veal infusion-dextrose broth to make the following concentrations (total volume 5 c.c.):

| | | |
|---|---|---|
| 1 : 50 | 1 : 10,000 | 1 : 5,000,000 |
| 1 : 100 | 1 : 50,000 | |
| 1 : 500 | 1 : 100,000 | |
| 1 : 1000 | 1 : 500,000 | |
| 1 : 5000 | 1 : 1,000,000 | |

Inoculated with yeast. All cultures showed luxuriant growth of yeast after twenty-four hours, showing that santonin has no inhibitive effect on the growth of this species of monilia. While it is understood that bacteria growing *in vitro* are not entirely in accord with their habits of growth *in vivo* this experiment is still of some significance.

Emetin has been recommended and endorsed by some as a therapeutic measure of value, not to the same extent as santonin, however. Here again it is very likely that any good derived from its use has been through mistaking the disease for amebic dysentery, or the prevalence of the two diseases in the same patient.

In 1921 Castellani[23] recommended the use of sodium bicarbonate in the treatment of the disease, and suggested large doses by mouth and intravenous injections of 2 to 4 per cent. solution in severe cases. The directions were to start with 1 dram three times a day by mouth, and increase gradually to 3 drams three times a day, continuing this dose for several weeks. Castellani thinks it has been of benefit to cases of sprue by decreasing the acidity of the gastric and intestinal contents, and in this way checking the growth of the monilia and other yeasts which notoriously grow so well in acid media. So far as I can tell from the literature no other observer has confirmed this work of Castellani. Others have relied upon a change in the character of the food, rather than the giving of drugs to alter the excessive acidity of the intestinal tract. Personally, I am opposed to giving large doses of sodium bicarbonate to combat hyperacidity of the gastric or intestinal tract. I believe, however, that there might be some benefit in giving other alkalis which will not produce alkalosis, *e. g.*, calcium carbonate. This drug might be of value in cases of sprue where the gastric contents show a hyperchlorhydria. According to the literature, the gastric contents in sprue may show a hyperchlorhydria, may be normal, may show a hypochlorhydria, or even an achlorhydria. In giving large doses of any alkali to patients whose gastric contents show an achlorhydria, harm might be done.

Pepsin and pancreatin, especially the latter, were highly recommended by the French physicians, Bertrand and Fontan.[24] Feris[25] also strenuously advocated its employment in the treatment of sprue. He claims that pancreatin acts not so much as a digestive ferment, as by stimulating the glands to whose function it corresponds. They believe that in many cases, with certain complications, these ferments may be of service, and as the indigestion is generally intestinal, pancreatin seems to be indicated rather than pepsin. T. R. Brown,[26] in 1916, reported extensive studies on the pancreatic ferments in sprue, finding all three ferments—trypsin, lipase, and diastase—absent. His technic is subject to some criticism because most of his studies were on the feces instead of the duodenal contents, as obtained through a

duodenal tube. Estimation of the pancreatic ferments in the feces is very difficult and subject to many inaccuracies. Therefore, in that part of Brown's work in which the feces only were used, and not the duodenal contents, there is some possibility of error in his studies. Few have confirmed his work.

Other observers, like Bastedo and Lamulener,[27] have been able to demonstrate activity in one of the ferments, trypsin, in both the duodenal contents and the feces.

Now comes the work of Silverman[28] reporting several cases of sprue, showing the presence of all three pancreatic ferments in the duodenal contents, obtained through the tube. He concludes that the appearance of an increased quantity of fat (between 40 and 47 per cent. according to the careful studies of Pratt and Spooner, and Harley and Goodbody) is not due to the alteration in structure or perversion of the pancreatic function, but to improper absorption of fat, brought about by a mild inflammation of the intestinal mucosa interfering with the absorptive power of the villi. He furthermore states that there is no relationship between the amount of hydrochloric acid in the stomach contents and the concentration of the pancreatic ferments in the intestine. Be this as it may, I believe that pancreatin is of benefit, and should be given, particularly in those cases associated with achlorhydria. It should be given in doses of 30 grains a day in keratin-coated pills or capsules.

Scott[29] reasoning from the report of tetany in sprue by Bovaird,[14] and the discovery of a lowered blood-calcium by Barrach and Murray[30] (confirmed by himself), advocated giving calcium. In addition to the calcium therapy he also advocated parathyroid extract, inasmuch as McCallum[31] has shown that the parathyroid glands are intimately associated with the development of tetany and the control of calcium metabolism, and perhaps the detoxication of poisons in the intestinal tract. Scott reports good results in several cases of sprue under this plan of treatment. Besides probably making up the calcium deficiency in the blood-serum in cases of sprue, there might come about additional benefits through the administration of calcium chlorid. According to Saxtorph[32] and Fishberg[33] in the treat-

ment of intestinal tuberculosis the intravenous administration of calcium chlorid was found of value. They believe that the good effect is due to the drug's inhibitory effect upon intestinal peristalsis, and its lessening of the irritability of the intestinal muscles. It is likely that calcium chlorid given intravenously, might be of benefit in the severer cases of sprue, solely for the purpose of controlling the diarrhea. The value of calcium therapy should be questioned by those familiar with the work of Ashford and Hernandez,[34] wherein they show that the low blood-serum calcium value in sprue is merely the result of a poor nutritional balance often occurring in other diseases besides sprue. Ashford does not believe that parathyroid extract has any effect when given by mouth, and when given hypodermically it produces only a temporary rise in the serum calcium. He believes the same rise consistently appears after dietetic treatment and vaccines, together or alone, and that there is never any need of the drug except in the rare cases complicated by tetany.

In the treatment of all types and all stages of the disease, diet is of pre-eminent importance, and is the one factor essential to success. It should be instituted early, adapted to the needs of the individual patient, and continued for months after the last active symptom has disappeared. Hence, the most important measure in the treatment of sprue is diet regulation in all cases, with or without rest in bed. All severer cases must be put to bed.

The object in dieting is to provide a plan of feeding with sufficient calories to maintain or increase the body weight, and at the same time to exclude as far as possible all starches and their derivatives, absolutely all sugar (saccharin in place of sugar when desired), and to limit fats to the minimum quantity compatible with savory cooking. The purpose of this plan of lowered carbohydrate feeding is to provide an unfavorable medium for bacterial growth, and to limit the formation of acetic, lactic, and butyric acids which Herter[35] has shown result from the breaking-up of carbohydrates in the intestinal tract. Fats should also be restricted on account of their laxative effect. In such intestinal conditions they are poorly digested and absorbed, hinder the

absorption of protein, favor putrefaction, and sometimes are irritants because of their liberation of fatty acids. The proteins should be increased largely on account of their ability to compensate nitrogenous waste, and because of their mineral content. Intestinal digestion is capable of compensating wholly, or largely, for the failure of protein digestion in the stomach.

The most commonly used foods are milk, meat, and fruits. Special diets which have been introduced in the treatment of sprue are:

1. The *milk cure*, introduced by Feris, in 1882,[36] is usually limited to the treatment of severe cases, combined with rest in bed. This consists of whole milk, boiled or unboiled, buttermilk, peptonized milk, acidophilus, or specially prepared milk, with a low fat, and a high protein content. Eight ounces are given every two hours, from 6 A. M. to 10 P. M., with directions to sip slowly, taking ten minutes to consume each glass. The quantity of milk should be gradually increased until 12 to 14 ounces are taken at each feeding, and continued three to five weeks.

2. The *meat diet*, introduced by Cantlie (also known as the Salesbury diet). In severe cases it may be begun with meat juice, pressed from slightly broiled meat, two tablespoonfuls every three hours. Later ½ to 2 pounds of scraped or chopped meat may be made into six servings, salted and cooked slightly, and one served every three hours. The meat should be given alone, but it rarely can be tolerated longer than a week or ten days. It may be given two days a week, and alternated with the milk treatment. Meat is easily assimilable, the residuum nearly approaching normal dejecta. With the meat diet, one or two cups of coffee daily may be permitted.

3. The *fruit diet*, suggested by Van der Burg in 1880,[37] permits various fruits—peaches, grapes, apples, goose berries, raspberries, blackberries, strawberries, cranberries, and ripe bananas. The great value of fruits in sprue is due to their ability to liberate certain vegetable acids supposedly inimical to bacterial growth. This is especially true of strawberries. An exclusive strawberry diet has been recommended, with directions to take 1 or 2 pounds a day, continuing until improvement is noted.

There is some objection to cranberries on account of the excessive acid present, requiring too much sugar to make them palatable. As the strawberry season is so short, bananas may be substituted, but they must be thoroughly ripe, or the unconverted starch will counteract any beneficial results. Well-ripened bananas contain an invert sugar which is easily digestible. Four to six bananas may be taken daily—raw, baked, or broiled.

It is interesting to note that liver, administered as liver soup, was a highly-recommended remedy, introduced in Ceylon many years ago. It can be understood now how this food may have been of value in severe cases associated with anemia, since liver has been found to be a specific in the treatment of pernicious anemia. The good effect in sprue is doubtless due to its influence upon blood regeneration, rather than upon diarrhea, and its supposed effect in increasing the flow of bile into the intestinal tract. Recently Ashford[38] reports upon the use of liver fraction in the treatment of the anemias of sprue, and he concludes that anemias of the pernicious type with high color index, and low red cell count (under 2,000,000) usually show definite improvement by such treatment, while those cases with anemia of the secondary type show no improvement.

Richardson and Klumpp[39] recently report their experience in the use of liver extract in the treatment of sprue. Their results were most favorable, for not only was the degree of the anemia lessened, but there was rapid improvement in the gastrointestinal symptoms. Basing an opinion upon their success in this case, they believe that not only can the associated anemia, but also the digestive symptoms of sprue be relieved by the use of liver extract, but they also add that it is too early to say whether or not this improvement will be permanent. This can be determined only after years of observation.

All of these diets have their good points, and in the treatment of the case presented here, a diet list was formulated composed of portions of all of the foods which had been tried by others and recommended as efficacious.

Milk could not be taken well by my patient because of the flatulence it produced. Acidophilus milk, as suggested by

Musser, caused even more discomfort. Finally, it was decided to try out a prepared low-fat, high-protein milk, Dryco, a powdered milk. This seemed to agree in every way. The completed diet list is as follows:

7.00 A. M.—An 8-ounce glass of protein milk.*

*Breakfast:*

1 or 2 sliced bananas, without cream or sugar; 1 or 2 eggs, soft boiled or poached, or a serving of broiled liver; 1 slice of unbuttered toast (hot), or 1 beaten biscuit; a small cup of coffee without cream or sugar (a ¼ grain tablet of Saxin may be used, if desired); an 8-ounce glass of protein milk.*

10.30 A. M.—An 8-ounce glass of protein milk.*

*Dinner:*

½ to 1 pound of tender steak, broiled with as little butter as possible, or ½ to 1 pound of scraped or chopped beef, or a serving of stewed chicken, or a serving of broiled sweetbreads†; 1 slice of hot unbuttered toast, or 1 beaten biscuit; 1 or 2 baked bananas; a serving of gelatin‡ (the bananas may be served in the gelatin if desired); an 8-ounce glass of protein milk.*

3.30 P. M.—An 8-ounce glass of protein milk.*

*Supper:*

A cup of broth or bouillon made from beef, chicken, or mutton; 1 or 2 raw bananas, or the same quantity baked or broiled; a small slice of hot unbuttered toast, or a beaten biscuit; a serving of gelatine; an 8-ounce glass of protein milk.*

8.00 P. M.—An 8-ounce glass of protein milk.*

Bananas must be thoroughly ripe and soft, but not in any degree spoiled, and may be served either raw, baked, or broiled, with a little butter. In season, strawberries (without sugar) may be used in place of bananas.

Only 1 small piece of toast or 1 beaten biscuit is allowed with each meal. Toast should be served hot so as to be palatable.

No cream or sugar is allowed. Use just as little butter as is possible in the preparation of broiled foods. Saccharin, or Saxin, ¼ grain tablets, may be substituted for sugar.

Above form of feeding should be continued until there is an improvement in character and frequency of stools. Then the quantity of protein milk

* Protein milk is made from Dryco, following directions on can—5 level tablespoons of Dryco to 1 glass of hot water.

† Vary meats from day to day.

‡ Use Knox's gelatin—do not use Jello.

may be increased to 12 ounces, and one or two vegetables from the following list allowed for dinner and supper:

| | | | |
|---|---|---|---|
| String beans | Spinach | Lima beans | All fresh (not canned) and well cooked. Vary from day to day. A serving consists of 2 to 3 tablespoons. |
| Okra | Turnips | Tomatoes | |
| Cauliflower | Carrots | Egg-plant | |
| Asparagus | Green peas | Squash | |

Raw tomatoes, lettuce, celery may be taken occasionally, with lemon juice.

Avoid all potatoes; yams; red and white beans; cow peas; sugar and flour bonbons; preserved fruits; fish of all sorts; pastry; pepper; sauces thickened with flour, etc.

Because of the achlorhydria in this case it was deemed best to continue the administration of dilute hydrochloric acid in doses of one teaspoonful in water after meals, in addition to the pancreatin in doses of 10 grains three times a day before meals. Under this medication, with a strict observance of the dietetic measures, the sprue symptoms have been controlled entirely. The patient is gaining weight and strength, the stools are well-formed, and rarely exceed two a day. She has returned to her home, and with a rest of two hours a day is able to carry on her duties as housekeeper.

Knowing the great proneness of sprue to show periods of improvement and then relapse, it is difficult to forecast a cure at this time. Should the patient continue to gain in weight and strength for some months, the blood approach normal, the stools continue well-formed and not exceed two a day, even if monilia are present in scant numbers, it might be considered a cure. The persistence of yeasts in the stools might place this patient in the class of a carrier. It is hoped that further study will show that the monilia have disappeared entirely from the stools, completing the cure in the strictest possible sense.*

* I am indebted for assistance in the bacteriologic study of this case to Dr. Anna Dean Dulaney, and for the illustrations to Mr. Joseph L. Scianni, Assistant Professor of Pathology and Bacteriology and Medical Artist, respectively, of the Pathological Institute, University of Tennessee.

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CLINIC OF DR. LEWIS M. GAINES

ATLANTA, GA.

## TWO CASES PRESENTING DIAGNOSTIC PROBLEMS IN ORGANIC NEUROLOGY

IN 1917 Gordon Holmes[1] reported a series of cases which presented a syndrome which was quite uniform and which as a whole differed from any previously described.

According to his description, at the onset there was general malaise and a rise of temperature ranging from 102° to 103° F. Pain in the legs and lower spine was usual on the second or third day and a day or two later muscular weakness in the lower extremities was soon followed by weakness in the arms. In addition it was observed that these cases developed along with the motor weakness described a bilateral facial paralysis, though no involvement of the tongue or laryngeal muscles. As a result of the facial involvement patients presented an expressionless countenance and an unnatural type of speech.

With the full development of the disease there was thus an extensive flaccid paralysis, often incomplete, abolished deep reflexes with retention of the skin reflexes, except that the plantars were usually absent.

He observed further that there was appreciation of touch, pain, heat, and cold with impairment of muscle and joint sense, and that the vesical sphincters were usually disturbed.

In three of these cases the blood and spinal fluid were both examined with negative result, although it might be noted that Viets[2] writing in 1927 and giving a report of 2 cases, finds the spinal fluid to be altered, at least in the severe cases which he has reviewed, in that the total protein content may be increased to ten or more times normal without other changes in the fluid.

Foster Kennedy,[3] in 1919, revived a term first proposed in 1898 by Mills, who at that time had recognized the fact that the

lesions in some cases of "peripheral neuritis" have involved the central as well as the peripheral nervous system. Feeling the appropriateness of this term to the syndrome as described by Gordon Holmes and as observed by him in 1917 and 1918 in France, Kennedy introduced the name "infective neuronitis" with the observation that these cases showed many of the "easily recognizable symptoms of acute polyneuritis . . . unmistakable evidences of involvement of the spinal roots and of the central nervous system as well."

There has not been entire agreement among authors who have reported cases of this disease since the appearance of Kennedy's original communication and various names have been proposed, such as "acute polyneuritis with facial diplegia," "facial diplegia in multiple neuritis," and in January, 1928 Brock and Ivimey[4] suggested the term "peripheral neuritis" to those cases in which only the distal parts of the nerve-trunks are affected. "Radiculitis" for involvement of the roots and "central neuritis" for involvement of cells and tracts of the neuraxis, the part to be designated by the appropriate adjective—spinal, medullary, pontile, etc.

In the matter of nomenclature in connection with the report of the case to be herewith presented, it appears to the writer that while the term "infective neuronitis" as suggested by Kennedy may have certain descriptive faults particularly in its pathologic implications, it is nevertheless far less cumbersome and sufficiently appropriate to recommend its adoption and will, therefore, be employed in this description.

Whatever name is finally agreed upon for this disease, it appears to be the general consensus of opinion that we are dealing with a group of cases in which either infective or toxic processes[1] are at work giving rise to pathologic changes in not only the peripheral nerves, but also the nerve-cells and tracts of the central nervous system. The disease has excited sufficient interest to have produced quite a respectable bibliography so that when Yudelson[5] published his contribution on the subject in February, 1926, he was able to present 67 references or articles on the disease gathered from the general literature. Since his presen-

tation, various other articles have appeared from time to time. One of the comparatively recent discussions of the disease by Viets summarizes admirably the clinical and pathologic features as follows:

"Clinically, the disease is characterized by the following features: The onset is usually acute, with fever; motor paralysis of the extremities appears early, is seldom complete, and the proximal part of the limb is more involved than the distal portions; sensory symptoms pass away quickly; the sphincters are often involved; the facial nerves are always involved, usually equally, and in all branches; the other cranial nerves are rarely affected; the deep reflexes are invariably lost; the disease may be fatal, but recovery takes place in a great majority of instances; complete restoration of function in non-fatal cases is to be expected within one or two years, although slight facial weakness, especially of the lower branches, may be permanent. Facial diplegia is the most characteristic sign of this disease, it is rarely complete, but there is practically always inability to close the eyes. Pathologic examination discloses marked secondary changes (chromatolysis) in the anterior horn cells of the spinal cord and in the facial nerve nuclei."

The following case observed by the writer presents all of the primary characteristics of this disease, although differing in certain details from some of the observed symptoms.

**Case I.**—A printer, twenty years of age, was first seen on January 9, 1928, complaining of complete facial paralysis, marked weakness of the legs, and to a lesser degree of the arms.

On January 3d six days before being seen, while at work, the patient noticed that he was unable to close his right eye and a short time later he could not move the entire right side of his face. However, he continued his work until six in the afternoon. Two days later he experienced a similar disturbance on the left side of his face so that he developed a total inability to move either side of the face or to close either eye. On this same day he found when he rose from bed in the morning that he was unable to walk without assistance on account of the marked weakness in both legs, which since that time has become more and more marked. On this day also he became nauseated and vomited once. There was slight headache but no fever on three occasions when his temperature was taken by his family physician. No visual disturbances were complained of, no diplopia, and no difficulty

in swallowing although the collection of food in the paralyzed cheeks made eating somewhat of a task. There was some difficulty in speech on account of the paralysis of the lips.

The patient noticed that there was a feeling of numbness and tingling in both arms and legs. There was no disturbance of the sphincters.

Although never robust the patient had always enjoyed good health and denied the use of alcohol and occurrence of any venereal disease.

About three weeks prior to the onset of his illness patient had complained of a cold in his head and on December 29th noticed a feeling of soreness in the right calf and foot when he walked, diagnosed by himself as "muscular rheumatism." Two days later the left leg and foot were similarly affected and these discomforts have continued.

The family history was excellent except that his mother died in 1915 with tuberculosis and a sister in 1924 with the same disease.

Examination showed a tall, pale, underweight man whose face showed a mask-like appearance, with total lack of expression. He was entirely unable to walk although able to move both legs in a feeble fashion.

His tongue was moderately coated and his breath quite foul. The pharynx was somewhat redder than normal, the tonsils small and without evidence of infection. At the time of the physical examination the pulse was 100, temperature 98⅘° F., respirations 20.

Examination of heart, lungs, and abdominal organs revealed no evidence of disease.

On neurologic examination there was a complete paralysis of both facial nerves, with loss of taste sensation on the anterior two thirds of the tongue on both sides. Speech was not disturbed except for difficulty in pronouncing the labials. There was no evidence of dysphagia. None of the other cranial nerves gave any evidence of disturbance.

There was a very marked weakness of both legs affecting all the muscle groups, both distal and proximal, and to a lesser extent both arms in a similar fashion. In addition to the subjective sensory disturbances described it was found that there was a marked degree of blunting to touch, pain, and temperature sense in the fingers and toes and to a less extent as one proceeded up the legs and arms gradually fading into normal sensation as the trunk was approached. There was apparently complete loss of joint sensation in all fingers and toes. There was also marked tenderness on pressure along the course of the nerve trunks both in the arms and legs.

The reflexes showed definite evidence of disturbance. The knee-jerks and ankle-jerks could not be obtained nor the deep reflexes of the upper extremities. The cremasteric reflexes were not obtained, but the abdominal reflexes were present. The pupillary reflexes were entirely normal.

January 10, 1928: Urinalysis: Light amber, slightly cloudy, specific gravity 1.010, acid reaction, no sugar. There was a heavy trace of albumin. Microscopic examination showed an occasional hyaline cast. No blood present and no other abnormality.

Blood count: Red blood-cells 4,220,000. White blood-cells, 11,000. Hemoglobin 88 per cent. Differential count: White blood-cells showed 30 per cent., lymphocytes 70 per cent., polymorphonuclear leukocytes.

January 16, 1928: Urinalysis: Slightly cloudy, specific gravity 1.022, acid reaction, no sugar, one plus albumin. No casts found on microscopic examination.

Both the Wassermann and Kahn tests were negative.

The spinal fluid contained 8 cells per cubic millimeter, was anticomplementary to the Wassermann test, showed a three plus increase in globulin and a sugar content of 77.8 mg. The colloidal gold curve was as follows: 4444555410.

The patient was kept under observation at the hospital from January 9th to 19th. During this period of time the temperature remained normal and his pulse rate varied from 88 to 110 while at complete rest in bed. Treatment was entirely symptomatic. His bowels were kept open with cascara, the mouth and throat were frequently cleansed and 2 per cent. mercurochrome was applied daily to the throat. He was given 1/40 grain of strychnin three times daily and bromid sedative at night. He was also given intravenously each twenty-four to forty-eight hours 31 grains of urotropin as there was a feeling that there was some type of infection present affecting the central nervous system, particularly the cord. He was also given small doses of potassium iodid. He was encouraged to take fluids very frequently and was given an abundant nourishing diet.

He was dismissed from the hospital on January 19th in about the same condition as on entrance. It was felt that if improvement occurred it would be slow and that he might carry out the same plan of treatment under his own physician.

On March 26, 1928 his father wrote that the patient had gradually improved after leaving the hospital and was able to walk a distance of one-fourth mile from his home to his shop and to resume some of his work as a printer.

He was last seen on April 27th, at which time there was very marked evidence of improvement, both in the distribution of the facial nerves and in the strength of his legs. All tenderness on pressure over the legs had disappeared except for a slight discomfort on pressing the left leg behind the knee. Faint remnants of the facial involvement were shown on attempts at closing the eyes. The paresthesias had all disappeared. The grip was good and equal in both hands and the patient walked without difficulty. The knee-jerk was barely obtained on the right and questionable on the left.

*Comment.*—The case described presents many of the characteristic features of neuronitis particularly the facial diplegia associated with evidences of peripheral neuritis.

In this case there was no rise of temperature during the time patient was under observation after the complete development of the disease nor was it possible to obtain a history of fever although the temperature was taken only three times. There was at no time in this case any disturbance of the sphincters which other writers have described as frequent in their cases. An in-

teresting observation in this case was the marked increase in the globulin content of the spinal fluid which otherwise showed no change from normal. There was a very marked leukocytosis and an albuminuria with an occasional hyaline cast on one examination. The pulse rate was moderately, but uniformly, elevated during the period of observation. We thus have some evidences aside from the neurologic aspects of the case that we are dealing with some type of general infecton.

The patient made a good recovery with, however, some traces of facial weakness remaining after a period of nearly four months. It is not felt that the therapy in this case had any particular bearing on the recovery.

Tumors of the gasserian ganglion are of sufficient rarity to merit considerable interest and at the same time present quite characteristic a syndrome. Frazier[6] made a careful review of the literature to 1918 and was able to find only 43 cases recorded, of which 30 were found at autopsy and 13 at operation. Of the latter, 10 were large inoperable growths. In but 3 was the tumor of such size that it could be removed. These 3 cases were recorded by Berg, Sachs, and Frazier. In Frazier's case operation was performed about three months after the onset of symptoms. Fifteen months after operation the patient exhibited no symptoms except paresthesias in the distribution of the trigeminal nerve on the affected side.

Most of the recorded cases have been those of inoperable tumors of the middle fossa. According to Hellsten the ganglion is peculiarly resistant to invasion of tumors practically all of which take their origin not from the ganglion itself, but from the dura or some other structure of the middle fossa involving the ganglion only coincidentlly. However, Frazier's operable case revealed an almond-shaped encapsulated growth overlying the ganglion and appearing to take its origin from it.

The great majority of the tumors of the ganglion are either sarcoma or endothelioma. Only one of the 43 cases was reported as fibroma.

The clinical features of Frazier's case are of sufficient interest

in connection with the case herewith reported to be summarized. A man aged fifty-three complained of pain in the distribution of the second division of the fifth nerve. At first the patient described the pain as "jumpy." Later it became more intense, and was associated with numbness in the upper lip and neuralgia above the left eye. The case was regarded as one of trigeminal neuralgia and two alcohol injections having failed to give relief, a radical operation was undertaken and tumor of the ganglion found.

While it is thus easy to confuse the symptoms of tumor with those of trigeminal neuralgia, it is quite striking that in tumor there is usually a combination of pain and anesthesia. The pain more often involves the entire distribution of the fifth nerve, is of greater intensity, and usually without the intervals of freedom so characteristic of tic douloureux. In addition the corneal reflex is often absent, the muscles of mastication show either weakness or paralysis on the affected side, and according to the literature, other cranial nerves may be implicated, especially the third and sixth.

There is sometimes difficulty in distinguishing between tumor of the gasserian ganglion and syphilis or tuberculous meningitis involving that structure. Appropriate and thorough examination, however, will usually lead to an avoidance of such confusion.

The first clinical manifestations of tumor of the ganglion from a study of the recorded cases are pain in the distribution of the fifth nerve usually in all three divisions simultaneously, although as in Frazier's case, the pain may be limited to distribution of only two divisions. The pain is severe and continuous with paroxysmal exacerbations. Objectively in the same distribution there is first hyperesthesia, later hypesthesia and hypalgesia and, finally, anesthesia and analgesia. In addition there may be noted trophic disturbances in the cornea. The motor branch of the fifth nerve is paralyzed sooner or later causing paresis or paralysis of the masseter, temporal, and pterygoid muscles.

It is of interest to note that in 1908 Spiller reported 2 cases in which the tumors were not primarily in the ganglion, but in each

case the ganglion was involved in the growth of large brain tumors primarily elsewhere. Both patients suffered severe pain in the distribution of the fifth nerve, and either hyperesthesia or anesthesia over the same distribution.

A year prior to Frazier's report, Sachs[7] reported a case in which at operation he found a smooth tumor about the size of a large cherry, apparently completely replacing the ganglion, and the tumor at the time was considered extradural. It subsequently developed, however, that although there was for six or seven weeks relief from pain, the tumor recurred and at autopsy it was found that the ganglion had been flattened out to paper thinness under the growth which was found on histologic examination to be endothelioma. From a study of his case, Sachs felt that severe continued pain in the distribution of the trigeminal nerve with paresis of the motor branches and anesthesia over the same sensory distribution justifies at once diagnosis of tumor of the gasserian ganglion.

The following case is reported on account of the rarity of the syndrome and also on account of the extreme rarity of the type of tumor found at operation.

**Case II.**—A farmer, sixty-nine years of age, whose home was in Florida, was first seen on August 15, 1927. His chief complaints were pain in the right temple and cheek and at times swelling below and to the outer side of the right eye.

The patient was in perfect health as far as he knows until about two years ago, at which time he had an attack which was diagnosed as paralysis, producing weakness of the right side of the face and to a very slight degree the right shoulder. He also noticed that the upper eyelid on the right could not be raised voluntarily and that this condition of ptosis remained until, following medical advice, he had some type of operation performed which had the effect of lifting the eyelid.

About two or three weeks after these disturbances he began to suffer from aching pain in the right temporal region for which he was given electrical and hydrotherapeutic treatments which had the apparent effect of giving relief for several weeks. The pain, however, returned over a larger distribution, affecting now not only the region of the temple but also the right supraorbital region beginning about the hair line and gradually descending to the eye, later involving the surface of the nose on the right, the area over the right antrum, and the roof of the mouth on the right side. He also felt that the orbit itself was the seat of more or less severe pain.

The patient returned to the Sanitarium where he had been given his

previous physiotherapy and took further similar treatment but without avail. Various sinuses were investigated and even opened without any positive pathologic findings or any relief to the sufferer.

The character of these pains was essentially that of a more or less constant ache with occasional superadded shooting darting pain over the distribution described.

In June, 1927 he noticed a slight though definite swelling over the right cheek and for several weeks thereafter he had a burning sensation over the right side of the head.

The pains thus described have, on the whole, gradually become more and more severe so that the patient has lost a great deal of sleep, appetite has become impaired, and his nutrition suffered. As a result he has grown weak and feeble and worn out with constant and prolonged suffering.

The patient for thirty years prior to the onset of his present complaint has been in excellent health. His teeth were all removed four years ago. He denies history of any type of venereal disease, has never used alcohol, and his habits in general have been temperate.

He has had malaria in mild form several times indefinitely in the past, an attack of typhoid fever many years ago as well as an attack of what was diagnosed as dengue fever. There have been no other serious illnesses since childhood. He has lived an outdoor life as a farmer and orange grower in Florida.

There is no history in the family of tuberculosis, cancer, or diabetes. Parents have been dead a number of years, cause unknown. Patient is married and his wife is living. She has never had any miscarriages. One child living and well, one died in infancy.

On physical examination the patient is a somewhat emaciated man whose expression of countenance and tone of voice indicate constant and prolonged suffering. At the time of examination the pain is particularly complained of in the supra- and infra-ortibal region on the right side. Over this area he also complains of abnormal sensations such as burning, feeling of pressure and numbness.

*Head.*—There is no evidence of nasal obstruction or tenderness over any of the sinuses. His teeth have all been removed. The throat is slightly congested. There are no enlargements to be seen or felt in any of the lymph-glands. The thyroid is small and gives no evidence of pathology.

*Chest* is well formed and the costal angle is wide. The lungs are resonant throughout and present no evidence of any abnormality. The heart is not enlarged, the sounds are clear and regular in rhythm. The pulse rate is 64 per minute, blood-pressure 124/70. The palpable vessels, including the radial and temporal vesels, are not markedly sclerotic.

*Abdomen* shows a scaphoid contour, presents no prominent veins, and no areas of tenderness or rigidity. The liver and spleen are not enlarged. There is no evidence of hernia.

*External Genitalia.*—No scars or discharge can be seen, and there is no enlargement of the lymph-glands of the groin.

*General Appearance.*—The general musculature of the body shows evidence of moderate emaciation with weakness. The skin is dry and somewhat

scaly, but there are no eruptions or gross evidences of any lesions. The spine is apparently normal on physical examination.

*Neurologic Examination.*—Cranial nerves:

I. Smell seems somewhat diminished on the right and normal on the left. There is, however, a slight nasal obstruction on the right which may account for the difference.

II. The eye-grounds show no evidence of choking of the disks or atrophy. There is no evidence of disturbance of the visual fields or hemianopsia on either side.

III, IV, VI. The pupils are equal and regular in contour and of normal size. They react to light both directly and consensually as well as on accommodation. The external ocular movements are performed normally in all directions. There is no nystagmus, exophthalmos, or ptosis although there is a history of ptosis on the right as well as a statement from the patient that there was diplopia three months previous, lasting one month.

V. Sensation of touch is definitely and markedly diminished over the distribution of the first and second divisions of the nerve. Patient apparently does not feel pin prick over this distribution. There is a complete loss of corneal reflex on account of a total anesthesia of the cornea.

The temporal and masseter muscles cannot be felt to contract on the right side so that in movements of the jaw there is a slight deviation to the right.

VII. There is a slight weakness on the right occipitofrontalis muscle on the right side. Otherwise there is no evidence of paralysis of the facial nerves.

VIII. Patient hears watch tick on the left on contact. Watch tick not heard on the right. There is a history of deafness on the right for forty years following typhoid fever.

IX. The movements of the palate are normal both right and left. The gag reflex is present and there is no disturbance of swallowing.

X. The pulse rate at time of neurologic examination was 80, blood-pressure 124/70. No history of vomiting and no evidence of disturbance of any of the branches of the vagus nerves.

XI. Normal.

XII. Normal.

*Cerebrum.*—There is a slight tremor of the outstretched hands but hardly more than would be expected from a feeble man of this age. There have been no evidences of disturbance of memory or of any of the higher faculties.

There is no paralysis of any muscle group and the strength seems good and equal on the two sides in the arms and legs.

Except as noted above there are no evidences of sensory disturbances, no astereognosis or adiadokokokinesia or disturbance of sensation of position of hands or feet.

There is no Romberg and the gait is within normal limits. There is no ataxia on any of the usual tests.

*Reflexes.*—The abdominal and cremasteric reflexes are equal and active on both sides. The deep reflexes of both the upper and lower extremities are equal both right and left. There is no ankle clonus or Babinski present. There is no evidence of past or present disturbance of the sphincters.

*Laboratory Examination.*—September 20, 1927.

Spinal Fluid.—Cell count 2 per cubic millimeter. Globulin-Pandy's test two plus, Ross-Jones test two plus. Sugar (Folin and Wu method) 58.8 mg. Colloidal gold test 0000000000.

Wassermann negative in all strengths. Kahn test negative.

September 16, 1927.—Blood Count.—Red blood-cells 4,650,000. White blood-cells 5800. Hemoglobin 88 per cent. Differential: Polymorphonuclears 66 per cent., small mononuclears 34 per cent.

September 25, 1927.—Urinalysis—Clear, amber, acid, specific gravity 1.022, no sugar, no albumin, no acetone or diacetic acid. Microscopic examination: Very occasional granular cast. Occasional white blood-cell or epithelial cell.

*x-Ray examination* of the skull revealed no evidence of any abnormality. *x*-Ray of all nasal accessory sinuses negative.

*Summary.*—An elderly man who enjoyed perfect health for thirty years developed about two years ago severe and more or less constant pain gradually increasing in intensity over the distribution of the first and second divisions of the fifth cranial nerve on the right side. Various efforts to give relief by physiotherapy as well as by various drugs have been without avail except temporarily.

At the time of examination the striking findings were anesthesia over the distribution of the first and second divisions of the fifth cranial nerve on the right side with evidence of paralysis of the motor division of the same nerve. A striking part of this finding was the demonstration of anesthesia of the cornea with consequent loss of the corneal reflex.

Dr. Charles E. Dowman of Atlanta, who saw this patient and made a careful study in consultation with the writer, felt that the picture presented by the above findings was strongly suggestive of tumor of the right gasserian ganglion, and suggested in the absence of any definite evidences of neurosyphilis that the gasserian ganglion be surgically explored.

Inasmuch as no evidence of syphilis could be found, operation was performed on September 27, 1927, by Dr. Dowman who made the following notes:

"Through the usual straight incision in the right temple region the underlying bone was exposed by separating the fascia and dividing it slightly on either side as it was attached to the zygoma and splitting the fibers of the temporal muscle. The bone was entered with the perforator and burr, and ronguered away well down under the temporal fossa toward the foramen spinosum. The dura was now elevated and the middle meningeal demonstrated, ligated, and divided. As an added precau-

tion the foramen spinosum was plugged with wax. The ganglion was now exposed and dissected free. A small tumor could be seen in the body of the ganglion. The sensory root was brought forward and freely dissected up from its bed. The third branch was demonstrated and divided. Then the second branch was similarly dealt with and finally the ganglion carefully dissected away from the site of the cavernous sinus, the last attachment being the ophthalmic division which was likewise divided. The whole removal was accomplished with practically no loss of blood whatsoever. The dura was now ballooned out by the injection of normal salt solution underneath it by means of a fine needle and syringe, and the wound was closed with several layers of fine interrupted silk sutures. The removed specimen showed the presence of a tumor which had the appearance of being a neurofibroma in the body of the ganglion itself.

"*Postoperative.*—Patient continues to complain of some pain in the right side of the face. It is felt, however, that this is due to the fact that he has had a good deal of morphin and withdrawal of the drug has caused a subconscious desire for the drug with the production of pain. It is felt that in time all soreness and pain will disappear from the face."

A report was received from the patient on November 29, 1927 that pain in the face had largely subsided, but that at times it feels as though it was "swollen and hard." The greatest distress at this time is the discomfort in the right eye which gives him pain when exposed to bright light and appears irritated. He has gained about 12 pounds in weight, and in general health is decidedly better.

A second report was received on June 6, 1928 in which it was stated that three months previously it was necessary to have the right eye removed on account of the discomfort and evidence of irritation which was evidently due to trophic disturbances. Patient has, however, suffered no more of the original pain of the face after a lapse of nine months.

*Pathologic Report.*—The tissue removed at operation was submitted to Dr. Everett L. Bishop, pathologist to the Albert

Steiner Clinic for Cancer and Allied Diseases, Atlanta, Georgia, who made the following report:

"Specimen without any fixation. The ganglion is slightly firm in its consistency, without gross evidence of hemorrhage,

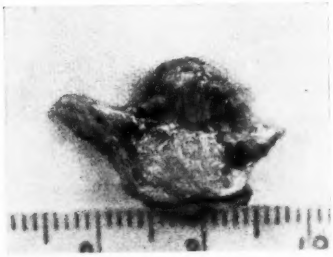

Fig. 202.—Ganglion with tumor in lower half.

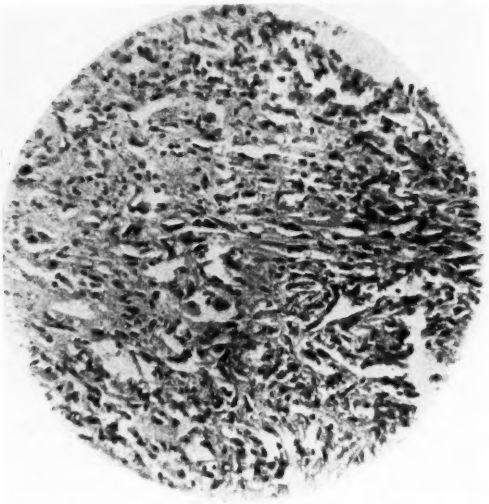

Fig. 203.—Section of tumor area. Cellular and fibrous structure.

necrosis, or infection. On the outer surface and lower border there is a rounded and slightly elevated mass, which is lighter in color than the remainder of the ganglion. This mass occupies almost one-half of the entire ganglion. Its surface is somewhat

ragged, and while circumscribed, there is no definite capsule. Cross-section shows this area to be without encapsulation and only poorly separated from the rest of the tissue.

"Sections show a very interesting structure. In the tumor area there is a well-marked cellular area, composed of medium sized hyperchromatic cells, and numerous fibers, running in various directions, with a slight tendency to form whorls. The proportion of cells to fibers is about equal, and the slow invasive character is evidenced by lack of complete demarcation. In

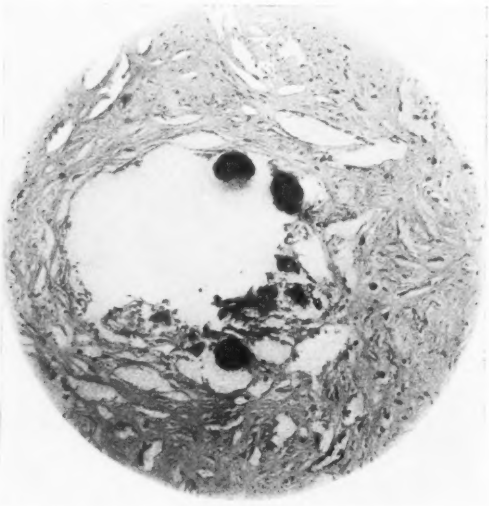

Fig. 204.—Section through ganglion. Hyalinization, calcification, and fiber degeneration.

the ganglion itself, there is marked hyalinization with calcification and degeneration of the nerve-fibers. A few collections of lymphocytes are observed at the tumor edge. No hemorrhage or necrosis seen.

"Diagnosis: Probable neurofibrosarcoma; low-grade malignancy; hyalinization and calcification of ganglion."

*Comment.*—It appears to be quite definite that the occurrence of severe and prolonged and more or less constant pain often

with periods of exacerbations in the distribution of the second or third branches of the fifth nerve should excite suspicion of the possibility of tumor of the gasserian ganglion, although this is rare in comparison to the frequency of trigeminal neuralgia. If examination reveals objective sensory changes in the painful areas the suspicion is further strengthened. These sensory changes may be at first hyperesthesia which, however, will give way in a relatively short time to hypesthesia and hypalgesia and still later to anesthesia. If in addition there is loss of corneal reflex and demonstrable weakness of the motor division of the fifth nerve the diagnosis of tumor may be safely made.

The case described presents the characteristic syndrome of tumor of the gasserian ganglion, and the tumor was found at operation. Successful removal of the tumor was done under local anesthesia, and the patient was given relief which has extended over a period of nine months, although removal of the eye was necessary some six months later on account of the trophic changes which occurred.

*Note.*—Since above report was written patient returned to Dr. Dowman on November 5, 1928 showing a loss of 20 pounds in weight, weak, and mentally irrational.

*x*-Ray showed evidence of necrotic bone in the skull, region of the erbit, whence the eye had been removed. Scrapings from this area were examined by Dr. E. L. Bishop, who gives the following report:

Sections show small alveoli, sheets and infiltrating strands of large cells of epithelial type, without fibers, moderately hyperchromatic and showing numerous mitoses. No hornification or pearls present. A considerable amount of connective tissue is present in the form of bulky strands separating the tumor cells.

Diagnosis: Epidermoid carcinoma; point of origin unknown.

Patient returned home on December 2, 1928, following as thorough curetting and drainage as possible, in an improved condition. The outlook, however, is considered most unfavorable.

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## CLINIC OF DR. GEORGE HERRMANN

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### CARDIOTHORACIC DISTRESS (TYPES). DIFFERENTIATION AND TREATMENT WITH ESPECIAL REFERENCE TO SYMPATHECTOMY

PAIN or discomfort in the precordial region is a common complaint. Precordial distress is, however, not always due to heart disease. In any discussion of this subject it behooves us to reconsider all the possible causes of precordial symptoms and to emphasize again the fact that extracardial mechanical factors may give rise to disturbing sensations that are commonly attributed to the heart. The clinical differentiation of this source of troublesome worry and of the various types of true heart pain is sometimes difficult, but always essential for rational treatment. A diagnosis of angina pectoris is of serious moment to any patient, especially if he is of the intelligent, temperamental, neurotic makeup, but it is likewise so even when he is of a stolid type. Only after a most searching clinical inquiry should such a conclusion be accepted, and even then it is often advisable to avoid the traditional term and to use the more modern and less awe-inspiring designation of "cardiac pain" which, I believe, is to be preferred.

Heart pain, even that of organic origin, varies much in its character, severity, duration, location, radiation, associated symptoms, precipitating factors, and in its response to treatment. Information on these points in the detailed clinical study of the patient is necessary for accurate differential diagnosis. The presence or absence of other physical abnormalities is, of course, important in the ultimate analysis, and classification of each case and in the outlining of a therapeutic régime.

In spite of the lucid classical description of Heberden, there has been considerable confusion as to just what clinical syn-

drome was to be included under the title of angina pectoris. It was noted by Heberden that in one type of case, spasmodic angina, strangling, constriction, or oppression predominated; while in another, paroxysmal dolor, or pain, under the sternum with more or less radiation predominated. In this symptom-complex there have been identified, within the last decade, two quite distinct and important syndromes. One type of pain is associated with thrombosis of a large branch of a coronary artery. In contrast to this, the other type presents no occlusion, but more or less sclerosis localized at the orifices or at the origins of the branches of the coronary arteries or no coronary changes whatsoever, but more or less aortic disease.

Still other more or less distinct and less serious mechanisms of cardiac pain have, in recent years, been identified and described. Among these we consider myocardial exhaustion pain of exertion in the presence of non-dilating coronary arteries, the pain of chronic valvular lesions, of adherent pericardium, of hypertension, of paroxysmal rapid rhythm disturbances, of anemia, or methemoglobinemia, of mechanical cardiac displacement origin, and pain on a psychogenic basis with or without associated endocrine disturbances. Pain in the chest from local disease processes in the spine or thoracic wall must of course not be lost sight of. The recognition of the type and mechanism of the disorder is paramount for successful therapeusis.

## ANGINA PECTORIS

The term "angina pectoris" has been retained for the traditional dramatic type of spasmodic heart pain attack. The *classical picture* will bear detailed consideration, for entirely satisfactory clinical differentiation of the morbid state or the abnormal physiology responsible for cardiac pain is at present not always possible.

The earlier, milder attacks of this symptom-complex are usually ignored or mistaken for disturbance in other organs, especially the stomach. The retrosternal position of the abnormal sensation is its chief characteristic and this along with a consideration of the provoking factors and the relieving factors

may give the clue. The abnormal sensation may be merely a heaviness or a burning that may simulate closely a pyrosis. The absence of physical signs of aortic or cardiac disease makes the diagnosis little more than a guess under these circumstances.

The typical paroxysmal, spasmodic attack of angina pectoris strikes precipitously and paroxysmally, transforming an apparently healthy, active individual into an immobile statuesque figure. The victim suffers an excruciating, burning, vise-like, crushing, squeezing, tearing, strangling, constricting, choking or oppressing pressure, heavy weight sensation, or a violent substernal pain at the level of the upper and middle third of the sternum. The alarming suddenness, the sense of imminent dissolution with the clear intellectual faculties give rise to an indescribable anguish, and anxiety. The distress seems unbearable, and the few *minutes* during the attack pass like hours.

Palpitation of the heart and a momentary sensation of suspended respiration may be felt, as may also epigastric fulness and nausea. The pain most characteristically radiates to the left shoulder, and down the inside of the left arm. It may transfix the left chest to the left back; it may pass into the neck, giving the sensation of strangulation, to the jaw on one or both sides, or to the face, or even to the top of the head. The pain in the secondary area may begin immediately or lag behind and may be spread over a wide area or be localized to the wrist, elbow, or inner upper arm. It may be sharp or it may be dull and aching—merely a heavy feeling associated with numbness and tingling. Soreness may remain for hours. Repeated attacks in close succession produce a status anginosus.

Accompanying vasomotor disturbances in the attack cause the patient's face to grow ashen pale, beads of perspiration to appear on his forehead, and his body to become clammy with perspiration and his extremities cold. He usually holds himself rigid in his steps with his hand over his heart. The respiration is seemingly unaltered; there is usually no dyspnea, though the breath is shallow or constrained because of distress. Eructations of gas and profuse micturition of pale urine may come at the end of an attack. The pulse and heart action are usually regular

and not at all affected though a slight rise in rate often occurs. The heart is usually at the upper limit of normal in size and only occasionally is it enlarged. The aortic dulness may or may not be slightly increased. An aortic systolic murmur and an accentuated aortic second sound in the presence of a normal or low blood-pressure are significant findings. The blood-pressure frequently, but not invariably, shows a rise during an attack; occasionally, it remains unchanged and sometimes there is a fall. The electrocardiogram frequently records changed or inverted T waves during an attack.

The dramatic relief afforded these patients by the use of nitrites or alcoholic preparations along with rest is characteristic, and the attack is always aborted by the specific drugs. The precipitating factors are emotion, anger, worry or fright, eating, overdistention, flatulence, exertion, and cold drafts. Bromids in full therapeutic doses will often break a succession of attacks by dulling the sensory reception of provocative stimuli and will reduce greatly the frequency of attacks when taken regularly in 1-gram (15-grain) doses. Soporifics, as chloral hydrate in 1-gm. (15-grain) doses at night or 3-gm. (5-grain) doses at intervals are especially effective in quieting nervous, hypertensive-individuals. Antispasmodics, as atropin in 0.5-mg. (1/100-grain) doses or, better still, homatropin brommethylate in 25-mg. ($\frac{1}{2}$-grain) doses, are often distinctly valuable in preventing and averting attacks. Vasodilators with persisting action, such as erythrol tetranitrate in 60-mg. ($\frac{3}{4}$-grain) doses, and theocin or theophyllin ethylenediamin 0.1 to 0.2 gm. ($1\frac{1}{2}$ to 3 grains) every four hours are of value. It is only after the attempt to find out the irritative precipitating factor and removal of it is unsuccessful and the rigid application of a therapeutic régim has failed that the radical measures to be discussed later are to be considered.

### CORONARY THROMBOSIS

Organic obstruction of the blood flow through a major branch of the coronary artery precipitates a clinical picture that is frequently difficult to differentiate from the classical syndrome. The individual prone to this sudden catastrophe

has usually had few if any symptoms of heart disease. Slight breathlessness and slight distress may or may not have been previously felt after a considerable effort. The victim is not infrequently convalescing from a respiratory infection of the influenzal type, or has an infectious focus that is or is not being treated.

Acute circulatory collapse may come on rapidly and be the outstanding symptom complex. An ashen gray sallowness, a saturnine pallor to actual cyanosis is present. Usually, however, a terrific agonizing pain predominates the picture. This pain differs from that of the classical syndrome chiefly in its persistence for hours and sometimes for days and weeks during which it is constantly present, but sometimes it presents waves of increased sharpness. Vasodilators, which act so dramatically in spasmodic pain, *fail* to relieve the pain of coronary obstruction. Morphin or pantopon in 30-mg. or $\frac{1}{2}$-grain doses is usually required to give any relief. Absolute rest during this critical period is of paramount importance, and should be secured as completely as possible. Measures to prevent the advance of the thrombosis or secondary thromboses are still only in the experimental stage. The classical status anginosus is almost exactly reproduced. In the true status anginosus there are however usually brief intervals of relief, and vasodilators are effective, but not so in that state in coronary occlusion.

The patient apparently soon learns that no fixed position, no tenseness of muscles does any good, and sometimes, not even exertion and eating affect the pain. Extreme weakness, however, often strikes the patient down, and makes him unable to move about. The power of speech may fail him. The pulse is usually very rapid or very slow, and is often irregular and often barely perceptible. The blood-pressure usually falls precipitously to dangerously low levels of 60 to 80 mm. of mercury. The heart sounds become very faint and muffled, and a pericardial friction rub may appear promptly or after several hours to a day. Within thirty-six hours a slight fever and a leukocytosis are present as a result of absorption of products of the necrosing infarcted myocardium. Electrocardiographic tracings show significant changes

in a large proportion, perhaps 75 per cent. of cases, but unfortunately not in all cases.

Disproportionate dyspnea, pulmonary edema with congestion and hemoptysis, cyanosis, vomiting, and hiccough are much more common in coronary thrombosis than in classical paroxysmal cardiac pain. The coronary thrombosis pain is also much more likely to be in the epigastrium and associated with other abdominal reflex states. The liver is more likely to be engorged after cardiac infarction, and further evidences of myocardial insufficiency as congestion and edema appear more rapidly. Death may come in or at a shorter or longer interval after the first breast pang.

The attack may subside, and with rest in bed the patient may recover. It is not uncommon after such a recovery to find that the patient is subject to cardiac pain on exertion. In this postcoronary thrombosis condition I have found that persistent vasodilators, such as theocin or theophyllin ethylenediamin increasing the coronary circulation, aid greatly in the reparative processes and increase the exercise tolerance and preclude the attack. The drugs should be given in 0.1 to 0.2 gm. ($1\frac{1}{2}$–3 grains) doses every three or four hours. Complete solution of the preparation is a most essential detail and is the deciding factor in the success or failure of the effectiveness of the drug.

### MYOCARDIAL EXHAUSTION PAIN

*Sclerosed coronary arteries* apparently cannot and do not respond with dilatation after exertion. The usual threefold coronary circulation required by the heart after exercise is not forthcoming and myocardial anoxemia and stretching fatigue result. Pain of a somewhat less sharp character, due to the so-called ischemia cordis intermittens, and accompanying distention of dilatation develop. Distress of this source is promptly relieved by rest. Vasodilators, the action of which persists, especially theocin or theophyllin ethylenediamin are of value in this condition.

*Certain advanced chronic valvular diseases*, especially mitral and

aortic stenosis and incompetency, may be associated with paroxysmal cardiac pain. In mitral stenosis the explanation of Sternberg seems rational. He found the fat pad about the circumflex branch of the coronary artery atrophied, presumably the result of pressure from the engorged left auricle, The vessel wall was somewhat thinned, so much so that any sudden increase in intra-auricular pressure could obliterate the artery or narrow it considerably and seriously embarrass the circulation in the heart. The low pulse-pressure present in mitral stenosis may also influence the coronary circulation. In the case of aortic stenosis, the low pulse-pressure may drop even lower with a temporary lag in a fatigued left heart muscle. It must also be remembered that the original rheumatic infection of the heart may have left some scars in and near the coronary arteries.

A heart bound down by *chronic internal* and *external fibrous pericardial adhesions* will have some disturbance of its coronary circulation, but primarily it will be exhausted from tugging against a fixed anchorage, giving rise to aching sensations over the heart.

The maintenance of a *hypertension* against a relentless peripheral resistance with an occasional, sudden, sharp rise in pressure precipitates chronic myocardial or acute temporary strain or heart exhaustion with the whole train of symptoms. Vasodilators will often promptly relieve this distress. Sometimes acute pulmonary edema supervenes and venesection is necessary.

Sudden *cardiac-mechanism disturbances*, such as paroxysmal auricular tachycardia, flutter, or block, especially those with very high rates or very low rates may be accompanied by sufficient intramyocardial circulatory disturbance to be associated with breast agony. *Grave anemia* and *methemoglobinemia* may at times be the only conditions present in a case to account for a precordial distress.

### BENIGN PRECORDIAL DISTRESS

One of the common disturbances associated with *precordial distress* seems to me to be *gastric flatulence*. It is remarkable how frequently physicians themselves become alarmed at the symptoms and present themselves with the condition. This

may be due in part to the ridicule that has been heaped upon the newspaper diagnosis of death as a result of acute indigestion in cases that undoubtedly have died of some type of coronary accident. It must, however, be remembered that a post-caval disturbance with eructation and even vomiting is not uncommon in a true heart pain attack. The usual symptoms consist of a sensation of heaviness in the right hypochondrium with or without an occasional, momentary, sharp, stabbing pain that goes through to the left back. The disturbance is usually noted after a heavy meal, and when the patient is seated or reclining. The erect position, standing, relieves the patient to some extent, but this is more true if the change in position is accompanied by gaseous eructations. Quick succussion palpation thrusts under the left costal margin aggravate the pain and thus serve as a confirmatory diagnostic test.

In spite of the fact that the patient has often learned that the taking of sodium bicarbonate facilitates the eructation of the gas from the stomach and relieves his distress, yet he worries until he is reassured and convinced of the origin and mechanism of the disturbance. The patient who suffers from this condition is usually of the hyperesthenic habitus with a transverse heart due to a high, flat diaphragm, a protuberant abdomen, and an increased intra-abdominal pressure. The symptoms are apparently produced in the pushing up of the dome of the left leaf of the diaphragm by the distended fundus of the stomach. The already transversely placed heart resting on the dome of the diaphragm may be shifted posteriorly. In this shifting a slight twisting of the heart, sufficient to embarrass slightly the coronary circulation, may take place, and give rise to symptoms, as will be explained later.

The predisposing habitus position of the heart, evidence of its shifting, the presence of abnormal gastric tympany in the right hypochondrium, extending Traube's semilunar area considerably, favor the diagnosis of a mechanical or postural cardiac embarrassment. The relief by change of position and belching, along with the absence of any discoverable cardiac or vascular abnormality, must be considered sufficient basis for the diagnosis

only however after every method of diagnosing the more serious condition has been exhausted. The danger of developing a habit aërophagia in the individual is considerable. The use of sodium bicarbonate to facilitate belching is not a desirable method of treatment, but potassium acid tartrate in 30-gm. (1-ounce) doses in hot water on arising or half an hour before meals is often of value in the control of flatulence. Dietary indiscretions, the use of flatulence producing vegetables or liquid foods as well as wind-sucking, if it is indulged in, should be corrected. There has been described a type of spasmodic precordial pain associated with abdominal conditions, and attributed to reflex segmental spinal cord disturbances. This is most often present in patients with gall-bladder pathology. This reflex group is the most confusing and the most difficult of diagnosis of all the types of cardiac pain. It is not infrequent that associated disease is present in the heart or great vessels and the gall-bladder.

*A toxic type of precordial distress* of more or less benign character, which is worthy of further comment, is that occurring in nicotin addicts. Persons, often under stress, smoke tobacco incessantly, usually inhaling the smoke deeply. Under these circumstances and often in more susceptible individuals with less abuse of the drug, there occur attacks of cardiac distress. The paroxysms may simulate quite closely the classical picture. Nicotine may act upon the cardiosympathetic nervous system and influence unfavorably the coronary circulation. It may be acting merely as an exciting factor in the presence of a latent process. Patients with frank coronary disease are often very chronic, inveterate tobacco addicts, and many observers are of the opinion that there is some causal relationship. This is more likely to be true for individuals who have an inherited tendency to coronary disease, for others can apparently indulge to excess with impunity. The chief characteristic of the so-called nicotin angina is its precipitation only after inhaling tobacco smoke and its prompt subsidence following the abstinence from tobacco. In some individuals with coronary disease, the inhalation of tobacco smoke will cause the onset of an attack of pain. The evidences of increased vagus tone, the slow irregular sinus

arrhythmia with or without ectopics or premature contractions, likewise promptly disappear after stopping the use of tobacco.

A *neurogenic form of more or less benign precordial distress* is described by individuals, usually females of a high-strung, *neurotic temperament*. The abnormal sensation varies from a heavy subcardiac ache to sharp, sudden, instantaneous precordial pains that momentarily transfix the thorax or radiate to the left axilla or left shoulder and sometimes even into the left arm. Ectopics or premature contractions of the heart are usually noted, and will account for the sudden, sharp, momentary pains in these very sensitive individuals. The patient is usually erethistic, restless, and emotional. Irregularities, tachycardia, palpitation, throbbing sensations, giddiness, and even vertigo are common symptoms which are, however, rarely present in one critically ill with the serious heart pain. The attacks are usually relieved by exertion and the patient has a good exercise tolerance. Except for the rhythm disturbance, the cardiovascular system is entirely negative in this condition. It is unfortunately also true that some cases of true anginal syndrome present very little abnormality on physical examination.

## THE MECHANISM OF PAIN

The *classical syndrome of angina pectoris*, as described, is the condition that warrants great respect as well as careful study for clear understanding and accurate differentiation. The symptom complex presents phenomena that are in a large measure neurologic. The explanations of the mechanism of the production of the cardiac pain is still for the most part theoretical.

Among the theories to account for cardiac pain, the vascular spasm idea with proximal stretching of the coronary artery and distal ischemia must still be considered tenable. Circular constrictions with proximal dilatation and distal blanching are to be seen in the retinal arteries in individuals subject to cerebral episodes. This is convincing evidence to me that such vascular phenomena do occur. Whether the pain is the result of the stimulation through the sensory nerves in the adventitia of the coronary artery or of the stretching of the ischemic ventricular

wall and its contained blood-vessels and accompanying nerves cannot be determined.

Allbutt's original theory attributed the stimulation to the involvement and stretching by increased blood-pressure of the aortic root, including the adventitial layers with their rich nerve-supply. The relief of pain with the onset of congestive failure and a falling blood-pressure may be an argument in favor of this theory. The venous congestion of the thebesian veins by passive stasis allowing more oxygenation of the myocardium may, however, be the explanation for the relief of the ischemic pain of coronary disease. Mackenzie's theory of the origin of the pain as the results of functional and organic disturbances of the coronary circulation seemingly has most adherents at the present time. The great bulk of the cases of heart pain can be explained most easily on this basis. The mechanism of sensory stimulation under these conditions may vary.

It is generally agreed that an ischemia and consequently an anoxemia of the heart-muscle results, but this brings us very little closer to the ultimate explanation of the pain. It does, however, give us a reason for the occasional sudden death of a patient in whom little or no pathology can be found in the heart. The disturbed circulation to the heart and the consequent poor oxygenation of the myocardium increase irritability and predispose to ventricular fibrillation, which once set up is practically always fatal. In most cases evidences are demonstrable supporting Mackenzie's idea of the association of the precordial distress with coronary changes as contrasted with Allbutt's aortic theory, in favor of which pathologic proofs are far less easily found.

## THE PAIN PATHWAYS

The pathways, however, that the impulses traverse from the aorta, coronary vessels, and heart to the cerebral cortex, where the sense of pain comes into consciousness, have been worked out fairly satisfactorily. The recent advances in this field have come about in large measure through the stimulating influence of surgical successes in the interruption of the sensory pathways.

There is still considerable difference of opinion and some confusion as to the details of the paths.

The coronary and the aortic deep and superficial plexuses are derived from sympathetic fibers, the so-called inferior, middle, and superior cardiothoracic nerves from the ganglia of the upper thoracic sympathetic cord. Afferent fibers to the central nervous system are apparently carried to the brain by way of the vagus and the depressor nerve, which is apparently intimately associated with it in the human being. Impulses go to the spinal cord through the white rami of the upper three or four thoracic, the stellate, the inferior, and the middle cervical ganglia. Vasomotor fibers to the coronary arteries have been shown to accompany the cardiothoracic nerves.

The radiation of the pain is easily explained on the segmental distribution of the different cardiac fibers. The usual spread is felt in the nerves from the upper four dorsal segments, but sometimes as low as the sixth dorsal and the seventh and eighth cervicals with pain in the neck and the back of the head. The first and third dorsals go to the retromanubrial region, the ulnar aspect of the forearm and arm, while the second dorsal segment is distributed to the inner aspect of the arm to the elbows.

## THE SURGICAL TREATMENT OF HEART PAIN. SOME INDICATIONS AND CONTRAINDICATIONS

Obviously, there are refractory cases of heart pain which do not respond to medical treatment. In the hands of a skilful therapist the unsuccessfully treated cases are relatively few in number. Among these unrelieved patients certain ones may be considerably benefited by a surgical blocking or severing of the nervous pathways.

The cases most favorable for surgical treatment from the medical standpoint are, of course, those with frequently recurring refractory paroxysmal pain of an excruciating nature, but without or with little evidence of organic disease in the aortic root, in the coronaries, or in the heart-muscle. The spasmodic type is the most amenable to neurosurgical treatment. Only where a dramatic nervous mechanism precipitates the

trouble is there much to be expected. In fact, aside from the classical, severe angina pectoris cases few, if any, sufferers should be subjected to the operation in hopes of relief.

Patients suffering from the pain of coronary thrombosis or postcardiac infarction angina make poor surgical risks, and the relief promised barely offsets the danger incurred. It is only in a persistent status anginosus or frequently recurring sharp attacks, which I have known to last as long as six weeks, occurring several times each night and each day, that the surgical procedure (and here perhaps alcohol injection rather than operation) should even be thought of, and then it is to be considered only as a palliative measure. I have, however, followed cases in which the palliative operation has been successfully done under adverse and contraindicatory conditions, and I have seen a life of veritable torture changed to one of comparative comfort. What the ultimate benefit may be in the matter of added years is difficult to estimate in such cases. The operation successfully over, the patient's days are certainly not shortened, and more than likely they are definitely lengthened. These patients who are usually submitted only to a palliative partial sympathectomy usually retain a dull reminder of their previous sharp pains. The great hazard, of course, is the operative manipulation, even though it be slight.

Attacks of pain in advanced coronary sclerosis cases, with ischemia cordis intermittens, in cases of valvular disease, adherent pericardium, hypertension, mechanism disturbances, grave anemias, in endocrine and in other benign conditions are not benefited by surgical treatment.

It is absolutely essential in every case of heart pain to establish as clearly as possible the provocative factor or factors, the pathologic anatomy, and the causes of the pathology. Removal of the precipitating irritation or attempts at correction of the functional defects incident to anatomic changes and the treatment of the etiologic factor, especially when this is syphilis, are often gratifying and accompanied by the relief of crises to such an extent that surgical intervention is usually unnecessary.

On the other hand, when the medical treatment fails as it

sometimes does, the surgical method should be resorted to, for the ultimate aim is to stop the painful crises. The attacks of pain are far from innocuous for the patient may die in any attack as a result of myocardial ischemia, anoxemia, and its fatal complication, ventricular fibrillation. This can occur without coronary thrombosis, and sometimes with little or no gross change in the coronary arteries or the heart. There lies in the crises of pain far more danger, I feel, than could possibly come from the removal of the pain which has been characterized as the "danger signal, the cry of anguish of an impoverished myocardium." Limitations must, of course, be indelibly impressed upon one who has been relieved of pain. It must be remembered that in the removal of sensory fibers, motor vasoconstrictors are also cut and the dangers of critical crises are less, but the disease process remains. It has even been suggested that repeated, painful crises may serve to exaggerate and hasten the basic pathologic processes.

The ideal case of heart pain for surgical intervention is usually the type that is a promising prospect for medical treatment, and as a rule these patients will not consider surgical treatment until medical therapy has proved useless. The surgeons prefer as subjects patients who have infrequent attacks, and who present no evidence of organic changes in the aortic root, the coronaries, or the heart valves.

In such patients it is true that the operative mortality will be kept low, and the therapeutic method will be less likely to fall into disrepute if the selection of cases be most rigid. If only the patients with the shorter attacks of pain at longer intervals and only on exertion of a considerable degree with no evidences of myocardial insufficiency between attacks and no electrocardiographic abnormalities be submitted to operation, the odds would be distinctly favorable for this method, or any other method of treatment that might be applied. Indeed if these restrictions are adhered to the number of surgically treated cases will of necessity be small and unrepresentative, for then there will undoubtedly be a preponderance of purely neurogenic cases. As a matter of fact, if the surgical treatment must be restricted to

such an extent, it adds comparatively little to our therapeutic armamentarium.

It is quite likely true that the surgical methods really offer considerable and must not be unduly restricted. The limits will be set after cases of varying grades of severity, carefully studied, and frankly reported, are critically analyzed. The studies of Levine and Newton, Cutler, Leriche and Fontaine are, of course, ably directed to this end.

Levine has, I believe, drawn up the qualifications all too rigidly. It is agreed that patients with coronary thrombosis pain during or shortly after the attack should not be subjected to extensive surgical procedures. However, I do believe that in the presence of intolerably agonizing status anginosus lasting for more than a week the less traumatizing procedures of Mandl or of Leriche are indicated from a purely humanitarian point of view.

The less severe, but nevertheless typical coronary thrombosis crises are, as a rule, relatively simply differentiated from the non-thrombotic seizures. The electrocardiogram is unfortunately not always typically abnormal, as has been argued. Occasionally one sees a status anginosus with repeated paroxysms which simulates mighty closely an attack of coronary thrombosis. On the other hand a stolid individual may suffer from a thrombosis which, from the description given of the pain, may be considered to be a mild spasmodic episode. I have had patients who had no pain whatsoever, but who presented extensive thrombosis of the coronary artery branches at autopsy. In general, however, the criteria hold fairly uniformly for this differentiation. The greatest danger is that a coronary thrombosis case will present itself with the radiation of pain to the abdomen, as is so common, and along with reflex somatic spasm, tenderness, fever, and leukocytosis will be considered an acute surgical abdomen and operated upon.[1]

Hypotension, alternation, great cardiac enlargement, distant blurted first sounds at the apex, gallop rhythm, or other grave mechanism disturbances, especially bundle-branch block,

[1] Medical Clinics of North America, 1927, 2, 719.

paroxysmal ventricular tachycardia, and high-grade fibrillation should make one hesitate and weigh carefully all the facts of the whole situation before advising surgical intervention for the relief of pain. To be sure, patients presenting any of these abnormalities are less safe surgical risks while a patient without them is a good risk. Selection on this rigid basis will keep the immediate operative mortality at an insignificant level, but it will also, I fear, deny the boon of relief to sufferers for many of whom life has become a painful burden. To these pain-tortured souls, exitus is looked forward to and existence is so miserable and agonizing that anything is welcomed.

**The Surgical Operation.**—The choice of the operative procedure must be guided by the condition of the patient. In the patient that measures up to the ideal requirements as a surgical risk, Cutler's statistics seem to indicate that the extensive ablations of the entire cervical sympathetic chain, including the first thoracic ganglion at once interrupting sensory and vasoconstrictor fibers, first on the left then on the right, offers the greatest hope of lasting relief. Relief was afforded even in the advanced severe type of the disorder. The complete unilateral procedure was well borne even by the patients with the serious type of the disturbance. In the most severe cases Cutler considers it wise to perform a partial sympathectomy, the removal of the superior cervical ganglion, division of the superior cardiac nerve, and that of the ramus communicans as a first stage to a subsequent complete sympathectomy. These two procedures have been most popular in this country. Partial cervical sympathectomy may be limited to the middle or inferior ganglion or to the stellate ganglion. Leriche has advocated the division of only the rami communicantes of the stellate ganglion through which pass the majority of the cardiosensory fibers to the spinal cord. The trunk directly above the stellate ganglion is usually also cut along with interruption of the vertebral nerve and the depressor fiber when it can be identified. The Viennese group advocated the section of the depressor nerve only on the basis that it is the chief afferent sensory nerve. The irregularity of the presence of this as a distinct cord, the difficulty of its identification, and the ques-

tionability of its physiologic sensory significance in human beings have contributed to the unpopularity of this procedure in this country. These partial procedures have been successful according to their sponsors, and they are advocated chiefly because of their simplicity, and the fact that they can be done with little or no trauma or danger to the patient, even in patients that are generally poor operative risks.

The paravertebral injection of alcohol into the sympathetic ganglia and their white rami has been used with success abroad and in this country. The method meets with the same objections that are raised against neural injections of alcohol in other painful disturbances. The temporary nature of the relief, the unsureness of the puncture method, and especially in the case of the cardiac patient, the impossibility of knowing just what is accomplished are facts that in my opinion contraindicate the method except in a temporary emergency where the patient's condition will not permit even a partial sympathectomy. Our greatest need now is the accumulation of data on carefully studied cases operated on by the various methods. It is quite likely that from it all we may learn something more about the cardiosympathetic system a subject about which we still have so much to learn.

## DISCUSSION OF CASES

The two cases that I wish to present are both of the type that are poor operative risks. They are not presented as spectacular therapeutic successes for they were not so. Furthermore, they are not to be taken as arguments for the universal application of sympathectomy regardless of the patient's condition. These cases should emphasize the fact that serious cases may be subjected to operation and even though the course may be stormy, a distinct and great relief of pain may be secured. The severity of the symptoms was such that surgical intervention was deemed advisable in each case in spite of apparent contraindications. It was, therefore, decided to present the facts to the patients and their families and allow them to consider the matter. Both of them actually preferred taking the great risk of a fatal issue rather than

to continue under existing conditions. Life had really become a painful burden.

The cases are of further interest in that both were females, and females with heart pain are much more uncommon than are males with the same trouble. Case I dated her trouble from an operation for gall-stones, which is unusual, while the second patient was seized while at hard work and apparently suffered a heart strain. The first patient presented a status anginosus and definite evidences of congestive heart-failure, while Case II had beginning congestive failure. Both had hypertension and enlarged hearts, aortic systolic murmurs, and abnormally metallic aortic second sounds, strongly suggesting aortitis at the root of the aorta, with the sclerotic processes more than likely involving the coronary arteries especially at their orifices. Abnormal electrocardiographic findings with persistent negative T waves were evidences of myocardial damage in both cases.

The second patient who was apparently the better risk and who was subjected to the least trauma and ablation, suffered the more stormy course after the operation, and had the more serious complication.

The postoperative courses were further evidence of the presence of advanced coronary disease most probably with healing myocardial infarction from the previous thromboses. In Case I there seemed to be little doubt of a thrombosis of the coronary having occurred. In Case II it is difficult to decide, however, whether or not coronary thrombosis had taken place, yet the stormy postoperative course with possible embolism was considered proof enough that such had been the case. The pain in each instance may be considered of the postcardiac infarction type, the first episode in each instance having been precipitated by a coronary thrombosis. The association of a glycosuria in the severe paroxysms of cardiac pain in the first case is indeed interesting and should have been more completely studied.

**Case I. Angina Pectoris, Probably Coronary Thrombosis with Status Anginosus, Greatly Relieved of Pain by Partial Sympathectomy.**—R. S., a married Russian Jewess aged forty-five years, came to my out-patient clinic because of pain in the heart of a constant, boring type with occasional sharp exacerbations, shortness of breath, and swelling of the dependent parts. She

ascribed the onset of her trouble to an operation for gall-stones eight years previously. One month following the operation she had the first attack of sharp, squeezing, vise-like precordial pain with a sense of suffocation, the attack lasting for a few minutes. There was radiation of the pain usually down the inner aspect of the left arm to the fingers and occasionally across to the right chest. A soreness remained in the parts for about ten minutes.

In subsequent attacks, which recurred at intervals of one to three weeks, the left arm became peculiarly abducted and spastic, and the pain, which for the first six months was negligible, became more knife-like. The attacks were always made worse by the cold of winter. Almost any emotional or exertional stimulus might prove to be a provocative factor. Amyl nitrite served to relieve the attacks for about seven years.

Her condition progressed relatively little and showed no definite change until about ten months before admission when, after physical overexertion, she suffered a sharp attack after which the pain persisted for two or three days instead of receding after a few minutes as it was wont to do. During this three-day period of constant pain, there were occasional, sharp exacerbations. She was free from attacks for some months following this episode.

Two months before presenting herself at the clinic she suffered a similar crisis from which she had not recovered at the time that she was admitted. From the onset of this second prolonged attack she had noted more ominous symptoms, such as shortness of breath on walking up a flight of stairs. This dyspnea was especially severe when sharp pain set in and was often relieved by standing up. Cyanosis, edema of the lungs and of the ankles, swelling of the abdomen, and tenderness over the liver were also present. Excruciatingly painful seizures occurred three to four times a day and sometimes as frequently during the night.

In searching her past history for relevant facts, little was to be found aside from a well-defined clinical picture of chronic cholecystitis and cholelithiasis. She had suffered from this for about sixteen months before she was operated upon. The onset of her heart pain was dated from this operation. There was no familial history of any similar disturbance. Her marital life of twenty-five years' duration had been hard in that she had had ten pregnancies, the seventh one of which ended in a miscarriage, and the eighth child had to be a forceps delivery. She had always had to do hard physical work in the rearing of her nine children. She was still menstruating. Nocturia occurred three to four times and diuria every half hour troubled her for years. Her extreme nervous irritability had made her subject to attacks on the slightest physical or nervous strain. Within two years she had dropped from a weight of 235 to 205 pounds, 20 pounds of which had been lost in the last two months as a result of the fact that the patient had eaten very little.

The *physical examination* during the attack of sharp pain presented unusual cyanosis and orthopnea in a more or less statuesque attitude with the left arm abducted, slightly flexed, and spastic, and she complained bitterly of the pain. With the relief from the pain the facies took on a less anxious expression, and the color changed to a heavy florid flush. The pupils were slightly irregular but reacted to light. A moderate neuroretinitis was present. The teeth that remained were carious, and the gums were suppurating

somewhat. The cervical glands were enlarged. The chest examination was difficult because of the heavy panniculus and the huge pendulous breasts.

The heart area of dulness was apparently considerably increased extending almost to the anterior axillary line. The apex impulse could not be seen or felt. An aortic systolic murmur, a loudly accentuated aortic second sound, a slight tachycardia, and numerous premature contractions were the only abnormalities that were detected. The brachial and radial arteries showed moderate sclerosis. The blood-pressure was greatly elevated and rose some during the attacks.

The *electrocardiograms*, taken in the service of Professor Frank N. Wilson to which the patient was transferred, showed slight left ventricular preponderance, ventricular premature contractions, inversion of T waves at first in lead I and then in I and II, and finally in all three leads with evidences of intraventricular block.

The abdomen was extremely obese with an apron-like fold over the symphysis. The scar of what had been a low gall-bladder incision was present. The extremities showed a slight subcutaneous edema.

The laboratory examinations were of no significance except for the finding of a heavy glycosuria during the crises of pain, but none between attacks. The non-protein nitrogen was normal, 33.7 mg. per 100 c.c. of blood. The Wassermann reaction was negative.

*Progress Notes.*—Morphin was required in addition to amyl nitrite and nitroglycerin for relief from the attacks. The patient was transferred to the surgical service for sympathectomy. Dr. F. A. Coller removed the *superior* and *middle cervical sympathetic ganglia* with the intervening cord. A mass of adjacent inflammatory cervical lymph-nodes made the operation difficult. After the operation Horner's syndrome (slight ptosis of the left eyelid, and pupillary dilatation) were present. The ganglia, on microscopic study, were found to show no degeneration and no abnormality except for a small collection of lymphocytes.

*Discussion of Case I.*—As a result of the operation the attacks of pain had lost their knife-like severity, and had changed considerably in character. Her pulse was down to 80 with the symptoms definitely relieved one month after operation. Three months after operation the patient returned to me because of attacks of heavy palpitation, choking sensation, and dyspnea, but with no return of the sharp pains. She was frequently aware of the dull precordial sensation of an aborted attack which before the operation was always associated with excruciating pain. She died in an attack three years after the operation.

**Case II. Angina Pectoris, Possibly Coronary Thrombosis, Relieved by Partial Sympathectomy, but Complicated by Postoperative Gangrene.**—W E., an American housewife, aged fifty-seven years had been seen by Professor Frank N. Wilson in consultation and referred to the hospital for

further study. She was admitted through my out-patient clinic to the medical ward service. Her complaints were pain and tenderness over the heart. The onset of her trouble had been precipitous. One year previous to admission while apparently in perfect health and able to do heavy work in her house and in the fields, she suffered, without warning, a severe, sharp substernal pain. This began in the region beneath the manubrium and radiated to the left chest and breast, down the ulnar side of the left arm and fingers, to both jaws and to the back of the neck and the spine. There was an accompanying sensation of "pounding" of the heart. The attack lasted about half an hour, and the medicines given her by her physician, although they caused a headache, were seemingly without effect. The pain apparently subsided with rest.

The disturbance recurred in short attacks at monthly intervals at first, and these were usually precipitated by walking and relieved by rest. Dyspnea on going upstairs gradually increased in severity. The seizures came at shorter and shorter intervals, were more easily precipitated, and were of a more severe nature. An unproductive cough and a fear of sudden dissolution often accompanied the attacks. For about two months a severe paroxysm had been suffered each day and often her night's sleep was interrupted by pain. The patient had the sensation of pins and needles in the left arm during and after the attacks of heart pain.

Her past history was irrelevant with regard to etiologic factors except for the fact that she had always done heavy labor. She had had frequent nosebleeds. An abscess of the ear had been drained twenty-five years previously and had not recurred. All the lower teeth had been removed and replaced for twenty years by a plate. Her menstrual periods had been normal and regular until she passed an uneventful climacteric at the age of fifty years. Her marital history was of interest in that she was her husband's third wife and had had some miscarriages, one stillbirth, but no living children. There had been no familial history of any similar disturbance or any cardiovascular disease.

The *physical examination* revealed a rather apathetic, obese woman who, however, showed considerable anxiety and orthopnea during her painful seizures. The left pupil was larger than the right, but there were no irregularities, and the reaction to light was prompt.

The chest movements were unhampered. The lungs were negative. The dorsal spine was tender to light percussion. Hyperesthesia of the skin was found in an area beneath the left breast and just to the left of the manubrium and the sternum and over and along the whole dorsal spine. The apex impulse could not be felt. The cardiac dulness extended 13 cm. to the left of the midsternal line. The retromanubrial dulness was not increased. The heart sounds were distant, the rhythm was regular, and the rate slightly increased. A short, rough systolic murmur was heard all over the precordium, but best in the aortic and secondary aortic areas. The aortic second sound was slightly accentuated and metallic. The electrocardiograms showed inverted T waves, indicating myocardial damage. The blood-pressure was 160 systolic and 84 diastolic. The peripheral arteries were distinctly sclerosed.

The abdominal panniculus was very thick. The liver and spleen could not be felt, and no tenderness was elicited below the costal margin. The reflexes were all normal in the extremities. There was no edema present.

The Wassermann reaction was found to be one plus on one occasion and was not repeated. The other laboratory studies were negative. The *x*-ray films showed pleural thickening at the right base. There was no fever present at any time while she was in the hospital.

*Progress Notes.*—During the first few days of hospitalization slight exertion in bed precipitated severe anginal attacks on several occasions. Nitroglycerin under the tongue in 0.5-mg. (1/100 grain) doses relieved the attack. Barbital in 0.6-gm. (10 grain) doses seemed to ward off night attacks.

The patient was transferred to surgery and operated upon by Dr. F. A. Coller. The middle cervical sympathetic ganglion was quickly exposed and skilfully removed. There was a minimum of trauma and the operation took very little time and seemed to be a simple, innocuous procedure. After the operation there was some pain in the surgical wound, but no return of the paroxysmal attacks of pain. It was observed by Dr. Frank N. Wilson that the hyperesthesia over the precordium was greatly decreased.

Three days after operation she was suddenly seized with a severe, sharp pain in the left foot and leg. The left foot became gangrenous. The complication was considered to be the result of an embolus from a mural thrombus in the left ventricle. Amputation was done through the lower third of the left thigh. The patient later developed erysipelas of the face, but recovered from this as well as the amputation. During the two months after operation she suffered no further anginal attacks.

Dr. C. V. Weller reported that the histologic study showed much fibrosis of the nerve sheaths, but he found no ganglion cells in the level sectioned in the pathologic laboratory. The left foot showed early anemic gangrene without infection. There was a thrombus in a large vein and evidence of congestion in others. The vessel walls were moderately thickened. The large peripheral nerve showed slight inflammatory infiltration.

*Discussion of Case II.*—The painful cardiac seizures were apparently stopped and did not recur in the two month period of observation. The complications were entirely unexpected, and this patient was considered a better operative risk than the first one, and less surgical ablation was done since only the middle cervical ganglion was extirpated. This was apparently enough, however, to give relief. The hospitalization must, of course, be given its share in any therapeutic evaluation. This is, however, a difficult factor to estimate. The amputation of the left leg was well borne, and this served further to restrict the patient's activities. An embolic hemiplegia often serves a similar purpose and hampers and restricts a patient who otherwise might not

accept his rigid limitations voluntarily. Thus, the apparent calamity often turns out to be a blessing. This patient in spite of all her troubles was firmly of the opinion that the relief afforded her by the operation far outweighed even the serious complications that she had suffered.

## GENERAL SUMMARY

The care requisite in the differential diagnosis of precordial pain is again emphasized and the chief characteristics and diagnostic criteria of various types of cardiac distress are outlined. The value of medical treatment must be kept in mind. The mechanism of pain and the pathways transversed by the sensation to the cortex are discussed.

The importance of distinguishing pain unassociated with detectable pathologic changes in the aorta and the heart from that which is apparently the result of gross cardiac changes is stressed.

The classical angina pectoris of Heberden without physical evidences of cardiac or vascular damage, the condition in which the neurologic factor is outstanding, is admittedly the most promising type of case for cure by sympathectomy. This type of case will often also respond to the removal of irritative, provocative conditions, and to the use of sedatives and antispasmodics. When, however, after a reasonable trial there is little or no response, the surgical treatment should be given careful consideration.

Many of the other types of precordial pain offer little hope for relief by surgical ablation of the cervical sympathetic chain and the cardiac sensory pathways. In many of these types of pain operative procedures are distinctly dangerous. The patient with a recent coronary thrombosis should not be mistaken for one with frequent paroxysmal visceromotor or viscerosensory attacks, and subjected to operation. Cyanosis, orthopnea, pulmonary edema, a falling blood-pressure, persistent pain, abnormal electrocardiographic findings, especially sharply inverted T waves in all leads or bundle block, must be considered as contra-

indications to any extensive surgical procedure under general anesthesia.

Exceptions to the general rules are, however, cases in which severe, persistent, excruciating pain, or rapidly repeated paroxysms make life such a torture that any risk is gladly accepted, for death is usually preferable to enduring such an existence of suffering. Under such circumstances partial sympathectomies under local anesthesia are to be considered and advised. Two examples of surgical intervention under unfavorable conditions are described.

Out of the maze of information that is being brought forth under this new stimulus of surgical sympathectomy of various types for the relief of pain should come some clear conception of the pathways of cardiac pain. The clue to the mechanism and etiologic factors concerned in the classical, apparently neurogenic angina pectoris may eventually be forthcoming. The method warrants our careful attention and study. To some of our patients it offers a great boon.

## CLINIC OF DR. W. R. HOUSTON

AUGUSTA, GA.

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### THE SPASMOGENIC APTITUDE

AFTER being away from my practice in America for five years, during this absence engaged in teaching medicine in the University of Yale-in-China, the first patient that I was called to see on my return was a trained nurse.

**Case I.**—She was a woman of thirty-three, and had nursed more or less continuously during the twelve years since her graduation, a good part of the time in institutional work. Some seven years before my seeing her she had had what she called a nervous breakdown, characterized, so far as I could learn, chiefly by anxious fears as to good intentions of persons about her. She attributed the insomnia and headaches from which she then suffered to malicious stories which she thought had been told about her. While after that she largely regained her poise, she was never quite to be convinced that her ideas about the malicious stories were pure obsessions.

At the time I saw her as a patient she was well nourished, inclining to plumpness, though pale and with blue rings under her eyes. She was brisk in movement, crisp and decisive in utterance. Much resistance was encountered in attempting to probe her emotional life. She proved to be an extreme introvert, buttoned-up in silences and reserves. There came to light the story of a love affair thwarted by the tongues of puritanical kinsfolk—a bitter grudge against a sister whose marriage had been favored. She had for a year been at home ministering with unswerving fidelity to those that had thwarted her, resentfully enduring the complacences of the sister whose lovable children were a reproach to her own spinsterhood. She was all for stern duty, all for repression of the gentler amenities, showing a prickly irritability against all kindly platitudes. She preferred to endure her sufferings alone and silently. She was only induced to receive medical advice through a devoted friend who had seen her wrestle all night with an enormously distended and painful abdomen, and had seen her fall on the bed suffering with violent chest pain—a pain described as coming on irrespective of effort, felt maximally over the precordium, radiating to the left shoulder and arm.

This highly intelligent neuropath was then suffering with painful colics and with a benign angina. The routine of gastro-intestinal examinations had shown nothing amiss. The examinations of the heart, physical, radiographic

as well as by the functional tests showed nothing. She spoke of being desperately tired, chronically and inveterately tired, though her demeanor would not have suggested it. No arguments however could induce her to slacken in her self-imposed routine of hard duties. Belladonna and the sedatives did little for her. Ultimately it became possible to put her in an entirely new environment where she once more found rest and comfort.

The obvious in this case is that we have a patient with a constitutionally inferior psychic makeup, that she has been exposed to failure, disappointment, and domestic difficulty, that she has driven herself to efforts beyond her strength, and that subsequently she has developed visceral neuroses of unusual intensity. The problem that interested me most, however, was why the neuroses took the form of spasm. Perhaps this question would never have suggested itself to me, but for my stay in China and my observation of the common ailments of the Chinese. Among the Chinese the everyday clinical picture that I have just sketched is not seen. I didn't see it. Excellent clinical observers who have been long in China tell me they did not see it. On reaching Peking I was told by Dr. Robertson who held the Chair of Medicine in The Peking Union Medical School that a case of angina pectoris had never been seen in a Chinese.

In China as elsewhere, all the types of heart disease are seen. Every day one can see rheumatic hearts, syphilitic aortitis, hyperthyroid hearts, fibrillators, heart lesions associated with the contracted kidney. The question is worth asking—does the fact that the Chinese are not subject to angina pectoris lighten the difficulty of comprehending the anginas we see here?

A collection has been made of as many as eighty different theories to explain the syndrome of angina pectoris. Those with which we are most familiar are that of Mackenzie, which, leaning on the conceptions of Head, would indicate that angina pectoris is not properly speaking a heart pain, but the expression of a series of viscerospinal reflexes, and which attributes the clamorous response of the cord to the violent excitation of the centripetal fibers—that of Allbutt who thinks that distention of the aorta is the key to the problem; the theory most generally taught —that of coronary thrombosis, to which the chief objection as a

sufficing explanation is that the majority of coronary thromboses, even with us, are not associated with pain. Probably a Chinese investigator would not have formulated anyone of these theories to explain this exotic syndrome to which Westerners are subject.

To quote from a recent monograph on angina pectoris by L. Gallavardin: "Angina pectoris constitutes in the household of cardio-aortic affections an exceptional manifestation. It might have been the case that all cardio-aortic affections were painful. It is not really clear why they are not all painful. But they are not. It is a matter of daily observation that valves of a patient's heart may become inflamed, or indurated, or shrink till they are unrecognizable, his aorta may be encrusted with calcareous deposits, may be covered with leprous ulcers, may be dilated as a whole, or may be distended locally and all that without his feeling the least pain. He may pass through all the stages of myocardial insufficiency, endure the refined martyrdom of all the dyspneas, drain every cup of anguish to the very last without having experienced any hint of what we call angina pectoris.

"In another person, on the contrary, whom we had had no reason to suspect of being a cardiopath, the initial symptom of heart disease will be a seizure of angina pectoris, and from that time on the repetitions of the seizure will constitute the entire disease.

"Granted that in both cases it is not the heart which pains. But why should the alarm bell in the spinal cord ring so violently and so precociously in the second case? And why in the first case, despite the most urgent warnings, should it fail to sound a note? After a hundred and fifty years of study we have not yet been able to give a satisfactory answer to this question —frightful index of the feebleness of our knowledge and the frailty of our means of information. Lacking other advantages, this humiliating uncertainty offers at least the advantage of keeping for the syndrome of angina the attraction of mystery ever inviolate and of retaining for it for a long time to come a place of honor in our discussions and our conventions."

The above citation from Gallavardin's monograph—a work notable for its keen logic and unflinching clinical objectivity—

would lead us to expect what actually develops, that the author is bound to no procrustean bed of theory in his exposition of the essential nature of the anginas. "The whole history of angina pectoris," he remarks elsewhere, "from the time of the first observations down to the assemblage of volumes that have appeared in recent years is marked by the same evil—to wit, the vain pursuit of the morbid entity that lies beneath the fugitive phenomena of the syndrome." It is from him, however, that I have taken the words "spasmogenic aptitude" that form the title of my remarks. A certain spasmogenic aptitude must be assumed to explain the incidence of anginal pain, the underlying pathology in any case being grave, slight, or none at all.

If the spasmogenic aptitude is great, a slight stimulus of neurogenic nature will suffice to evoke the spasm with its characteristic pain. If the spasmogenic aptitude is absent, the utmost stimulus will fail to evoke the spasm. Between these extremes, stimuli will provoke spasm in accordance with the ratio that exists between spasmogenic aptitude and the vigor of the stimulus.

The term "spasmogenic aptitude" would seem to have about the same meaning as spasmophilia, but spasmophilia has attached to it certain connotations relating to calcium metabolism and the activity of the parathyroids. We would like to say that the Chinese do not have angina pectoris because they lack the spasmogenic aptitude without saying that their parathyroids are inactive. We would like to say that the majority of our cardiopaths do not have angina pectoris and that the minority that suffers from angina suffer by reason of this spasmogenic aptitude without meaning that they are deficient in calcium.

To recur to the patient whom we are considering we will recall that she not only had anginal pain, but several attacks of abdominal pain that kept her busy all night with enemas and stupes working for relief. If a person has a constitutional aptitude toward spasm in unstriped muscles it might be expected that unstriped muscles in different systems would be affected. This expectation is quite generally realized. When I look back over the patients I have seen suffering from the benign anginas

it has generally been true that they have had other spasms. Two young men that I have under observation now have had attacks of pylorospasm and colic in addition to the anginal attacks. By the same logic people who notably lack the spasmogenic aptitude might be expected not only to be free from angina pectoris, but to show an immunity from spasm in other systems. During my years in China I was struck with the different picture that the neuroses generally presented, as well as by the difference in the nervous reaction in the presence of organic irritation. I regret that my abrupt exit from the scene at the time of the Communistic upheaval there prevented my pursuing the subject statistically. Since my return I have written to The Peking Union Medical College, one of the outstanding medical institutions of the world, to get information. Dr. H. C. Chang, an important member of their medical staff has reviewed for me the statistics of the past seven years. Among 24,884 patients analyzed, those that could be considered to suffer from spasm of unstriped muscle were strikingly few—about 1 per thousand. He studied the digestive tube, the urinary tract, the blood-vessels, and the vagina. There were no cases of Raynaud's disease, 1 case of spasmodic stricture of the male urethra. There was 1 case of pylorospasm in a premature infant, and 8 in adults that might be called functional.

In contrast with this situation, complaint of spasm with us seems to be the most usual of all the complaints that the internist who sees chronic disease meets with. When I returned to work here the impression I got of the frequency of spasm as the presenting symptom was overwhelming. I first felt at home in my work again when I began to see patients coming in with the complaint of spasm in every sort of tube in the body. My work as an internist is not perhaps entirely representative as it runs rather to neurology and gastro-enterology.

A very large proportion of the chronic cases that have come to me for study have shown evidence of the spasmogenic aptitude as the chief or as an important factor in the clinical picture. Let me cite only a few of many instances.

**Case II. Spasm of Gullet.**—B. X., aged thirty-seven years, 6 feet, 2 nches in height, weight 176, of rugged muscular build. Manages a tailoring shop. Was treated by me twelve years ago, when he was a farmer, for severe discomfort after eating and fear of taking food. At that time he weighed only 118 pounds. He made a prompt and good recovery. Being ambitious he pressed ahead in the world until he had now come to have a good business.

He entered my consulting room with his collar unbuttoned and his necktie knotted loosely far below its proper place. This he said was due to choking. Anything touching his throat made him choke. Shaving was most distressing to him and he could by no means lie in a barber's chair. What distressed him most was riding in a car. As soon as he put his foot on the clutch his throat clutched. In busy traffic his plight was worse.

The trouble had come on suddenly about a year previously. While riding at fifty miles an hour toward his country home he felt his throat close up. He stopped the car and pulled out to the side of the road. His heart was beating tumultuously. Ever since his life had been miserable. His sleep became broken. He lost 15 pounds in weight. His discomfort after eating returned. He recalled the maxims and measures that had helped him before but they failed him.

He was physically sound every way and treatment by moral persuasion and encouragement, an ordered life, and mild sedatives soon restored him to comfort. This seems to have been an intensified form of globus—perhaps the commonest of all the spasms.

**Case III. Spasm of the Cardia.**—C. D., a vigorous man of forty-eight, a county policeman, gave a history of having had three attacks of inability to swallow food or any water. Attempts at swallowing were followed by immediate regurgitation. The attacks had lasted each time nearly two days. In his last attack he started to the city, a sixty mile drive, to see me. When he entered he still thought he could not swallow. A semisolid barium meal and a stomach-tube passed through to his stomach without any evidence of obstruction. The attack—apparently one of spasm of the cardia—has passed away. This type of spasm, unlike most, causes frequently no pain, merely offering an obstacle to taking food. General physical examination—no important findings.

**Case IV. Spasm of the Midesophagus.**—J. M., a brisk business man of thirty-four, alert in bearing, lively in speech, of slender but adequate build. He comes with a ready made diagnosis of peptic ulcer. Examination shows moderate hypermotility and hyperacidity of the stomach, but no filling defects and a good cap. His complaints, it turns out, are not of the stomach, but of substernal pain—a sudden pain as of a huge ball forming in the breast, swelling as if to burst, accompanied by a tightening in the throat and a feeling of impending disaster. He must stop still till the pain subsides. The pain is not related to taking food. It may come when he is drinking water, or again without any provocation when he is walking along the street.

This kind of pain, while it is not easy to prove the fact, objectively is almost surely a spasm of the esophagus. A hot drink tends to relieve it. Rest and relaxing treatment cure it fairly easily.

**Case V. Spasm of the Pylorus.**—A healthy looking farmer, aged sixty-two years, who had given no previous history of ill-health, especially no history of indigestion, was operated on for a primary cancer of the kidney pelvis, which had produced profuse hematuria. After removal of the kidney his convalescence was prolonged and difficult on account of severe bronchitis and mental confusion. About three weeks after the operation, just as he seemed to be getting back to normal the operative wound having given no trouble at any time, he suddenly sank and died within fifteen minutes. Autopsy disclosed indurated ulcer of the stomach, which had perforated, perforation leading at the same time to profuse hemorrhage which was the immediate cause of death.

This case is cited to call attention to grave ulcer of the stomach without symptom of spasm. It is generally conceded that the usual pain of peptic ulcer, strictly related in time to the taking of food, runs parallel with the spasm. There is, of course, a different type of pain when localized peritonitis comes as a complication. There are some analogies between the spasmodic pain of peptic ulcer and the pain of angina. In both cases there may be grave lesions without pain; and just as there may be angina without cardiac pathology, so there may be, and frequently is, pain of pylorospasm without ulcer.

The common finding is pain closely related to the presence of ulcer. Von Bergmann's theory that ulcer is secondary to spasm, while it fails to account for the silent ulcers, at least calls our attention to the importance of spasm in prolonging and intensifying the ulcer. Certainly the medical treatment of peptic ulcer is almost entirely concerned with the problem of combating spasm. Where spasm can be abolished, as is easily done in most cases, the ulcer quite generally heals.

Passing on down the digestive tube to the ileum we find that this part of the alimentary tract, biologically the most primitive and physiologically the most essential to life and seeming to be also the most stable part of the digestive system, is relatively immune to diseases of all sorts—a fortunate thing in view of its inaccessibility to investigation. While the occasional cases of intussusception may lead us to suspect spasm there is no clear evidence of spasm of the ileum as a common clinical occurrence.

**Case V. Spasm of the Colon.**—Married woman, aged thirty-one years, two children, for twelve years had been subject to severe attacks of abdom-

inal pain mostly in the ascending colon, sometimes in the transverse, not specially constipated. She thinks that an attack of colic led to premature birth of her first child. She has had several attacks of urticaria in the past. Three years ago the pains in the right colon were so severe and accompanied with so much tenderness that an appendectomy and Waugh's colopexy were done. This procedure was successful in relieving right-sided pain which has never recurred.

Though she is of a lively temperament and socially active, and despite a not wholly well adjusted home environment, she was fairly well after her operation until she contracted amebic dysentery. This was accompanied with severe pain in the left colon and a very vigorous treatment with emetin and stovarsol contributed to reduce her nervous potential. She finally became free of all evidences of dysentery except spasmodic pain which tormented her cruelly at the most unexpected times. When seen four months ago superficial ulceration was found in the upper rectum and lower sigmoid. The junction of descending and pelvic colon was very sensitive to pressure.

Despite rest and sedatives, together with careful attention to diet and evacuation of the colon, the spasm occurred at intervals of ten days or two weeks with the greatest violence. The best relief from the excruciating pain was found in large doses of chloral, which seems to be our most reliable antispasmodic. A more recent repetition of the *x*-ray and sigmoidoscopic examinations shows the mucous membrane now healthy, the haustra of the colon well defined. Two barium enemas showed the colon capable of good dilatation at the point of maximal tenderness. The pathology seems to be very slight but the spasms have not yet been overcome.

There is something in the way in which the spasm recurred suddenly after a period of relative well being that made one think of epileptic seizures, the more so as this disease had been manifested in the family history.

**Case VI. Spasm of the Bladder Mechanism.**—A young man of twenty-six years, a gentleman farmer, entered complaining of spasms in the colon. These were evidently immediately due to misuse of cathartics. Five months previously he had been operated on for perforated duodenal ulcer from which he made a good recovery so that he had evidently had spasm in the pyloric region. His father had also had a long siege with pylorospasm and gastric ulcer with hemorrhage, which finally required surgical treatment. This young man next appeared with a spasmodic stricture. He had no history of, and no evidence of, venereal disease. The spasms in the cut-off muscle were somewhat painful, but the chief difficulty was interference with micturition. In the course of time with forced feeding and rest he became free from all his spasms, though the usual treatment with sounds helped the spasm in the urinary tract.

**Case VII.**—A Jewish merchant, aged thirty years, bachelor, in sound general health. Complained of urinary frequency whenever he was in company, though not at other times. He had gradually shut himself off from theaters and all social gatherings. He never called at the homes of his friends on account of this embarrassing symptom. It was obvious in this case that the troubles were purely psychogenic.

**Case VIII.**—A housewife, aged sixty-two, a grandmother. Her children and grandchildren had left her in charge of a large, nearly empty home where she maintained a vigorous activity. In the past she had had periods of spasmodic trouble. At one time she had choking spells in which she coughed and choked, though without pathology in the throat. She had suffered with cold feet and hands, leading her to resort to excessive devices to keep warm. She had had nervous diarrheas. She had also been operated on for a duodenal ulcer. Her chief complaint at present was spasm of the bladder with much tenesmus.

She looked like a healthy woman and physical examination was practically negative except for an insignificant trigonitis. This was the second attack of painful spasm of the bladder that she had had; the first was relieved by going away from home for a restful visit, the second by rest in the hospital and a less active life when she returned to her home.

Four female patients of this general type have come under my observation recently. Spasm of the bladder is sometimes a very distressing and intractable symptom, again very capricious, staying away for long periods and returning whenever nervous excitement develops. Two of these patients had been submitted to the passage of ureteral sounds with more harm than good. All of the cases had had some instrumental treatment without definite benefit. Treatment directed to the general nervous condition was the only successful one.

**Case IX. Spasm of Blood-vessels.**—A husky, broad-shouldered Irishman whose muscles fitted him for the heaviest manual labor was employed as a clerk working at night. Convalescing from an attack of malarial fever he fell into an anxiety neurosis, characterized chiefly by marked agoraphobia, and claustrophobia. He also had phobias about his physical condition which led to a loss of 20 pounds through the fear of eating.

During the early part of this trouble his blood-pressure went to 220/120 and stayed high for some time. Fortunately he was very suggestable and in a short time overcame all his fear by the simple process of doing the things he was afraid to do. His blood-pressure returned to normal.

This type of case illustrating psychogenic arterial hypertension is illustrated in the paper of Dr. C. L. Eshlemann that appears in this volume. It seems that there is a gradual transition from transient hypertension to continuous hypertension in certain instances, and that continuous hypertension leads ultimately to damaged arterioles and grave lesions of the vital organs. It has been sufficiently demonstrated that hypertension

of whatever kind is mediated through the vegetative nervous system.

Essential hypertension is unknown in China. Cases of hypertension, though uncommon there, are found associated with the contracted kidney, but the arteriosclerotic kidney does not seem to be caused by prolonged hypertension.

I saw in China one interesting exception to this general rule. A supervisor of nurses, aged thirty-five, who had been trained many years in America and had acquired the American quickness and alertness of movement, in striking contrast to the slow, easy ways of the average Chinese nurse, developed an essential hypertension and severe headaches. She had so alienated herself from the native Chinese attitude that she used to refer to "these Chinese" with their trifling ways. Her thorough-going and energetic demeanor had brought her into an essential hypertension. In a large service extending over four years this was the only case I ever saw of essential hypertension in a Chinese.

It is well known that the Chinese normal blood-pressure is 100/65, and observations have been made to show that when they live in America they acquire our normal pressure. Dr. J. H. Foster of the Medical College of Yale-in-China who studied the blood-pressure of a group of foreigners living in China for a number of years, found that their blood-pressure generally in the course of time came down to the Chinese level. Other observers have noted the same phenomenon. When a foreigner living in the interior of China acquires an essential hypertension it is generally obvious that the sufferer is a person living in a state of antagonism with his environment—one who has come to China to teach everything and learn nothing.

There is a question whether a continuous and tonic spasm such as we see in essential hypertension should be classified with the briefer spasm that we have been considering. We may remember, however, that the digestive tract also has its prolonged tonic spasm as seen for example, in cardiospasm and much more commonly in the tonic spasm of spastic constipation.

I will report one illustrative case of the type that is often called chronic biliousness.

**Case X.**—H. W., aged thirty-three years, a go-getter high-tension salesman. His manner of speech and behavior suggested the crisp vivacity of the fox terrier combined with something of the tenacity of the bulldog. Since the age of twenty-two he has been a sufferer from abdominal pain and obdurate constipation. At one time he worked along the idea that he was being poisoned by the contents of the bowels. He found that a heavy dose of calomel gave relief from his symptoms for a few days. This is quite a common experience with sufferers from the spasmogenic aptitude. The nausea and malaise that attends the taking of a large dose of calomel produces a relaxation of the spasmodic tendency which may last sometime, just as the briefer relaxation that accompanies vomiting will relax the spasm of croup.

During only one period of this twelve years did the patient feel entirely well. This was during his period of service in the army. At that time he was entrusted with managing the gymnastic exercises in the Company that he was attached to. He was free from the sense of personal responsibility. He gained 35 pounds in weight and for the first time in some years was entirely free of constipation.

On his return to civil life his old disturbances gradually came back, loss of weight—all that he had gained and 10 pounds more—the constipation became inveterate and intractable. He suffered with severe headaches, which quite often disappeared a few moments after the bowels were emptied.

Pain was felt at times in the region of the cecum. The cecum was often distended with gas and tender at times. This pain was not very severe but had led him to seek a diagnosis of appendicitis on more than one occasion and finally to get it. Dr. Crane, the surgeon to whom he was finally referred, did not believe in the diagnosis of appendicitis, but in view of his having a very mobile right colon decided to do a Waugh's colopexy. The pathologist reported a normal appendix. When convalescing from the operation I saw him still suffering more or less from his old symptoms, the tendency to biliousness as he had been accustomed to call it. The operation, plus the course of mental and physical hygiene suggested, served to free him from his biliousness and put him back to the condition of health that he enjoyed while in the army.

There are many other conditions constantly met with that arouse speculation as to what part the spasmogenic aptitude may play in their pathogenesis, for example, croup in children and asthma. Migraine has often been considered a spasm of the blood-vessel, but we have not the time to take up these debatable conditions which lie on the fringes of the subject. I have one very interesting case which seems to speak quite clearly for a neurogenic spasm of the ureter without there being any serious question of stricture or twisting. The left-sided pain came only at the menstrual period, it could be reproduced by dilating the renal pelvis, it had led to an exploration of the ab-

domen without relief. Though the ureter admitted without difficulty the largest sounds the spasm reappeared at the next period. In the realm of gynecology it seems quite probable that many instances of dysmenorrhea may be referred to the spasmogenic aptitude.

## DISCUSSION

We have cited briefly a number of cases showing an aptitude to spasm in the unstriped muscle, in the circular coats of the various conducting tubes, in the alimentary tract, the urinary tract, the blood-vessels. We have called attention to the very great frequency of spasm in our people as contrasted with the relative infrequency of this symptom among the Chinese.

What can we say as to the significance of this observation? It is quite certain that in some instances the spasm could be directly referred to psychic states—were directly traceable to low nerve potential—to chronic fatigue; others to disturbances in the emotional life, or to the force of suggestion. There are cases in which there is present, it is true, a minimal degree of morbid pathology, but in which the pathology is quite inadequate to explain the violence of the spasmodic reaction, cases which contrast strangely with others having an extensive pathology of the same type, yet without spasm.

It may be taken as an accepted dictum of physiology that the circular coats of these tubes, the contraction of which produce the painful spasms referred to, whatever inherent quality of contractility they may possess contract in the main as the result of stimulus coming through the vegetative nervous system. The vegetative nervous system is the proximal cause of the trouble. At this point we inevitably begin to think of the theories of Eppinger and Hess. Is it vagotonia or sympathicotonia that we have been discussing all along? Without attempting to rehearse the arguments pro and con, it will be enough to say that the analysis of this question by Cannon, Langdon Brown, and others suffices to make it clear that no such schematic division as Eppinger and Hess have undertaken can be maintained. We often in the same person, at the same time, meet with spasms that belong to the sympathetic and parasympathetic overaction

—for example, pylorospasm (vagus), and urethral spasm (sympathetic). My feeling is that it will be more cautious, perhaps more correct, to think of spasm in a global way without trying to lay stress on niceties of bridle-rein in the many-spanned team. The function of these contracting mechanisms are doubtless projected on the central nervous system as an entirety. They are best to be thought of in the way in which we think of a spastic monoplegia due to a cortical lesion, that is taking little account of the several nerves that further flexion or extension.

If we grant that these spasms, whether paroxysmal or continuous, directly result from the action of the vegetative nervous system on the ring muscles we are forced to push the question further. What stimulates the vegetative nervous mechanism? The trigger is often local irritation, but as we have seen, this factor is often trivial, often undiscoverable, and hence we are obliged to feel that the main emphasis is to be put upon a certain hypersensitiveness to stimulus—what we have called the spasmogenic aptitude. We may ask, is this aptitude to be explained by some alteration in the chemistry of the body fluids? Efforts have been made to seek a chemical explanation. Dr. Ralph Majors has thought that an increase in creatinin-like substances was a constant accompaniment of essential hypertension and hence probably a cause. Others have considered the relations of visceral spasm to calcium metabolism. Those that are enthusiastic about the rôle of allergy as an etiologic factor ascribe much of the symptomatology of spasm to the atopens. There has been considerable vague speculation as to the importance of dietetic factors—as that a high protein diet predisposes to spasm, that excess of purin bodies in the diet is spasmogenic.

Perhaps all these theories could best be tested by recurring to our original paradigm. Do we see that the Chinese, notably lacking as they are in the spasmogenic aptitude, take few purins in their diet, consume little protein, go without much salt, have a plentiful calcium store in the blood, are relatively immune to allergic influences? A definitive answer to these questions might end much vain speculation. I regret that I am not provided with any final answer. So far as concerns the diet of the Chinese, I

believe, that while the poor take much less protein than we do and that vegetable protein, the well to do seem to eat as much meat as we do. Their cooking is elaborate and epicurean; ours by comparison is simple and unsophisticated, but the proportions of the essential components of diet among the more affluent Chinese is about the same as with us. As between the coolie in China, living on his rice and herbs, and the wealthy gentleman sitting down daily to a highly-seasoned menu of fish, fowl, mutton, pork, and beef no differences were observed in blood-pressure or other tendency to spasm. Further, the considerable group of occidentals living in the interior of China, whose blood-pressure sank to the Chinese level took practically the same diet as at home. There are seen in China many morbid conditions related to diet and metabolism—beriberi, rickets, xerophthalmia, on the one hand; diabetes and obesity on the other, but the spasmogenic aptitude is lacking.

It is attractive to muse on the possibility of some endocrine imbalance as representing the kind of chemical stimulus that acts on the vegetative nerves to provoke spasm. Are Chinese lacking in adrenal or in pituitary? Have the sufferers from visceral spasm an over supply of incretion from these glands? One thinks of the hairlessness of the Chinese breast and limbs, of his irenic disposition, but then one reflects on the absence of any constant marking of the spasmogenics with evidence of glandular excess and this line of conjecture loses itself.

A far more helpful lead in our search for a way of thinking about the essential nature of the spasmogenic aptitude is offered by the promise of psychologic analysis to reveal the primum movens. Ah yes, the Chinese lack the spasmogenic aptitude—placid, gentle, peaceloving—Buddhist—their ideal, the serene calm of Amida Buddha, with closed lids and folded hands—symbol, the lotus flower scarcely swaying over the still pool. We are so well acquainted with the high-bred Chinese in fiction, a monstrous mixture of atrocity, suppleness and suavity with his jade ornaments, his silken embroideries, his naïve disarming smile, behind which diabolism lurks—so assured and self contained that his pulse never quickens as he plans and executes

nameless cruelites. Surely his "bowels are not moved with compassion" as were the bowels of the Hebrews in ancient days and yet are today. It is easy to see why he never has angina or hyperpiesis—this tranquil quietist. It is easy to see why the red, hairy, wassail-quaffing, fighting barbarian from the west has the spasmogenic aptitude ready set upon minimal provocation to tighten its coils on him.

The trouble about all this is that it is fiction and fiction unusually disdainful of fact. When I first reached China I was told by Dr. Andrew Woods, Professor of Neurology in the Peking Union Medical College, that the Chinese were the most neurotic people in the world—more neurotic than Jews. My impression from observation was that their neuroses were preponderantly of the anxiety type in motivation, with symptoms in a general way of flaccid rather than spasmodic type, impotence, a sense that the genitals were shrinking away, transient paralyses of the extremities and so on.

In a recent paper in which he examined the causes of essential hypertension Dr. Herman Mosenthal expressed the opinion that it was not to be explained by chemical factors—that psychic factors were paramount in the etiology of this condition. This is particularly interesting because Dr. Mosenthal's work has been much along biochemical lines. He concludes by saying that the remedy for essential hypertension is calm.

The Chinese are not calm. If one went no further than to take a boat up the Yangtse River and to see and hear the struggling vociferous mob that swarm on the landing stage, the yells and objurgations of the boatmen in their sampans alongside he would dismiss the notion of applying the word "calm" to Chinese. Highly excitable and unendingly noisy he would call them. What the natural unsophisticated Chinese most loves is din and stir. The word "reh-nao"—literally hot bustle—one of the most used words in their language is constantly employed to describe all that is most pleasing in a city or locality. As the great ship drew alongside the dock at Seattle the most striking impression I got of my own country after four years absence was of the unwonted calm and noiselessness. Quite true the Chinese culti-

vate an ideal that inculcates calm and impassivity, just as we cultivate an ideal that teaches us to turn the other cheek, but in either case the religious teaching is upheld because it runs exactly counter to the innate bent.

We seem to have fallen on contradictions—just what is calm? The first association is with surface—calm sea, calm lake, calm visage—"calm yourself"—that is, reinforce your inhibitions and acquire external immobility. We have all seen essential hypertensives who outwardly were calmness itself. It must be that there is an inner calm, a deep calm, possible even in conjunction with superficial agitation.

A Chinese expressed the fundamental distinction between Chinese and occidental psychology by saying that the occidental when meeting with a difficulty tries to remove it, making a change in the external environment, an external adjustment—the Chinese finds it easier to make an internal adjustment—to change his soul to an attitude of acceptance. When the axle on the wheelbarrow squeaks an squeals we grease it. The Chinese wheelbarrows are never greased. They can be heard half a mile away. We say the screeching is intolerable—they accept it. If we stay in China long enough we, most of us, learn to accept things, and our normal systolic pressure becomes, as the Chinese is, about 100. If the Chinese live in America long enough they learn our habit of protest and non-acceptance, and their normal blood-pressure rises to our level.

The suggestion naturally arises—if we would avoid spasm be as the Chinese. True enough, but all our ideals of progress and development are bound up with the zestful spirit of protest and non-acceptance. We must realize that a low reaction threshold to spasm is not an unmixed good. The spasms from which we suffer are the "defects of our qualities," a precious racial asset become excessive and gone awry.

What to think of the essence of the spasmogenic aptitude. We have found ourselves forced to place it in the dim category of constitutional defects—constitution made up, as it is, of something inborn, something taken from environment.

The psychic, which means the most delicate of the mechan-

isms by which we make our adjustments to environment, is the best approach we have to the task of ameliorating evils that come from a spasmogenic aptitude. In addition to re-education, reassurance and moralization, we may reckon rest, quietude, isolation from social irritation to the measures that are chiefly psychic in their mode of action. A well balanced consideration of all that makes for mental and physical hygiene comes first. Sedatives of the barbital group, or the bromids, may delay the onset of spasmodic attacks, may break the habit of spasm. Drugs of the belladonna group acting through the vegetative nervous system are occasionally effective; it is surprising what enormous doses are sometimes tolerated by obstinate spasmogenics. Last I mention what is usually considered first and not infrequently to the exclusion of more fundamental factors—the removal of local sources of irritation. Undoubtedly there are cases where this therapy demands first consideration and is the only factor which is of enough importance to require serious attention. Confronted with gall-stones or renal colic due to the passage of stones nobody will think about spasmogenic aptitude. On the other hand many distressing therapeutic miscarriages result from the overemphasis of local conditions, the continuous hammering away at local therapy where the pathology is very slight. The result is often to accentuate the tendency to spasm.

In conclusion I can but feel that much benefit may be derived from our laying firm hold of the question of spasmogenic aptitude as a concrete clinical entity. It is conceivable that were we to concentrate on unriddling the nature of the spasmogenic aptitude we might end the "vain pursuit of morbid entity under the fugitive appearances of the syndromes." Under which conditions does the spasmogenic aptitude appear, under which it is absent? If one wishes to refer a student to his text-books to look up this subject it is hard to find the chapter and page for him. He will find something under the captions of hysteria and neurasthenia, globus hystericus and so on. Most of his information will be found under the sections devoted to the heart, circulation, respiration, and gastro-intestinal tract, and in the monographs on gynecology and genito-urinary diseases. A grasp of the con-

stitutional nature of the spasmogenic aptitude, of the tendency to spasm as a distinctive thing clinically, might not merely stimulate a more complete study of its nature and bearings, but it might serve to warn the too mechanistically minded to look beyond the organ in spasm, to look to the patient, his constitution, his temperament, the threads that bind him to his fellows.

# CLINIC OF DR. CHAILLE JAMISON*

NEW ORLEANS, LA.

## A CASE OF PERNICIOUS ANEMIA[1]

PERRY McCaleb, Baton Rouge, La., a negro laborer, fifty-two years old, was admitted to Medical Service Six of the Charity Hospital, New Orleans, on October 24, 1928 complaining of weakness, swelling of the legs and shortness of breath on exertion. Last January he first noticed that the ankles were swollen and that he could not walk fast because of dypnea. The edema has increased and a numb sensation has developed in the right foot. His appetite and digestion have been good; he has two or three semisolid stools daily, *the tongue has never been sore.* His urinary function has been normal except for occasional nocturia. He has had a slight cough recently on exertion, but there has been no sputum. He sleeps well. His usual weight has been around 185 pounds, but he thinks he has lost a few pounds recently. For the six months preceding the appearance of his symptoms he was employed by a natural gas company, and attributes his illness to the inhalation of gas.

Except for occasional attacks of mild sore throat, no serious sickness has occurred in the past; he had gonorrhea once in his youth and denies other venereal infection. He is married and his wife has had fifteen living children and three stillbirths; nine of the children are living and well, and six have died of causes unknown to the patient. He has a good home and plenty to eat; he does not drink, but smokes to excess. He comes of a robust and healthy family; his father and one brother died of causes which he does not know, but one brother and six sisters are living and well.

*Examination.*—A dark, chocolate-colored negro male adult, with the features, hair, and skull typical of his race. He was lying flat in bed, apparently comfortable, and answered questions promptly and clearly. He was well-developed and well-nourished, but the skin, which was dry and inelastic, pitted slightly on pressure. The radial artery was palpable, and the pulse firm, regular, and of good volume, with a rate of 70. Temperature 97.9° F. and respirations 15. The conjunctiva was very pale; the sclera showed the brown pigmentation so common in older negroes, but no jaundice. The pupils were equal and responded to light and distance normally. The general condition of the oral cavity was good for a negro; a few teeth were missing, but the others were in fair condition. The tonsils could not be seen. The

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tongue appeared entirely normal. The mucous membrane of the entire cavity was pale; there was no pigmentation. The head presented nothing else of note. The neck, the thoracic wall, and the lungs were negative. The heart was not enlarged; there was a systolic murmur, which was not constant and which was not transmitted, accompanying the first sound; the second sounds were clear and not accentuated. The blood-pressure was 122/90. The abdomen was very much distended, ovoid in shape, and tense to the palpating hand; no masses, tumor, or organs could be felt, and there was no tenderness or rigidity. The classical physical signs of free fluid in the peritoneum were easily elicited. The genitals were negative. The lower extremities were edematous to the knees. The patella reflex could not be elicited. There was no local or general adenopathy.

*Clinical Course.*—The patient's general condition improved rapidly and steadily. The edema disappeared in about ten days. The improvement in the blood-picture was very prompt, as shown by the blood reports, and was typical of the response to be expected from liver feeding in pernicious anemia. There has been no fever and little change in pulse rate or blood-pressure. The ascites has shown no improvement. Two gallons of a clear straw fluid was removed by paracentesis November 12, 1928; the fluid rapidly reaccumulated and 4500 c.c. was removed November 24, 1928 and a like amount on December 12, 1928. At the present time, December 22, 1928, the abdomen is again much enlarged. No therapy other than liver feeding and rest was instituted. The use of novarsurol was considered but not instituted. The fluid output was much in excess of the intake during the early part of the patient's treatment.

*Laboratory Examinations.*—Blood Examinations:

11/ 2/28: Total red cells per cubic millimeter, 990,000. Hemoglobin, 40 per cent.
Total white cells per cubic millimeter 6250. Color index, 2.2.
Differential count: S. M. 50; L. M. 0.; E. 0., B. 0., N. 50.

11/ 6/28:* Total red cells per cubic millimeter 1,420,000. Hemoglobin 41 per cent. or 5.82 gm.
Hematocrit volume 18.5 per cent.
Average corpuscular volume 130.3 cubic microns.
Average corpuscular hemoglobin 41 x 10.
Percentage of hemoglobin in average cell 31.5 per cent.
Volume index 1.59. Color index 1.43. Saturation index 0.9.
Price Jones count average of 130 cells, 8.7 microns.
Numerous megaloblasts; some normoblasts; reticulocytes.
Anisocytosis and poikilocytosis very marked.

11/16/28*: Total red cells per cubic millimeter 2,340,000. Hemoglobin 56 per cent or 7.96 gm.
Hematocrit volume 28.8 per cent.
Average corpuscular volume 123 cubic microns.
Average corpuscular hemoglobin 34 x 10.
Percentage of hemoglobin in average cell 27.6 per cent.
Volume index 1.50. Color index 1.19. Saturation index 0.79

* These examinations were made by Dr. Max Wintrobe.

11/26/28*: Total red cells per cubic millimeter 4,010,000. Hemoglobin 85 per cent. or 12.2 gm.
Hematocrit volume 41.4 per cent.
Average corpuscular volume 103 cubic microns.
Average corpuscular hemoglobin 30.4 x 10.
Percentage of hemoglobin in average cell 29.5 per cent.
Volume index 1.26. Color index 1.06. Saturation index 0.84.

12/ 7/28*: Total red cells per cubic millimeter 4,200,000. Hemoglobin 75 per cent. or 11 gm.
Hematocrit volume 37.7 per cent.
Average corpuscular volume 89.8 cubic microns.
Average corpuscular hemoglobin 21.2 x 10.
Percentage of hemoglobin in average cell 29.2 per cent.
Volume index 1.1. Color index 0.92. Saturation index 0.83.
Price Jones count average of 100 cells, 8.26 microns.

10/25/28: Blood chemistry:

| | |
|---|---|
| Total non-protein nitrogen | 31.5 |
| Urea nitrogen | 16.0 |
| Creatinin | 1.2 |
| Blood-sugar | 93.0 |
| Chlorids | 0.53 |

12/ 4/28: Van den Bergh reaction: Direct, negative; indirect, 0.3 unit. icterus index 8.

11/ 7/28: Platelet count 43,000. Coagulation time three minutes, fifteen seconds.
Bleeding time three and a half minutes. Blood Wassermann reaction negative.

Feces: No parasites or ova found.

Spinal fluid: Wassermann negative; cell count 6; globulin negative; colloidal gold curve unsatisfactory.

Urine: Five examinations of the urine were negative chemically and microscopically. The reaction was constantly acid to litmus; the specific gravity varied from 1.002 to 1.014. Neither urobilin nor urobilinogen was found. The phenolsulphonephthalein test was 25 per cent. of the dye in two hours at the time of the patient's admission, but has steadily increased.

11/14/28: Ascitic fluid cell count 6; globulin 3 plus; no organisms found by culture or direct examination.

11/26/28: Ascitic fluid cell count 40; globulin 4 plus; no organisms found by culture or direct examination. There were 102 mg. of sugar per 100 c.c. of fluid.

10/25/28: Gastric contents: Total acidity 15; free HCl 0; no occult blood.

11/ 8/28: Gastric contents: Total acidity 15; free HCl 0; no occult blood.

11/ 9/28*: Electrocardiogram: PR interval 0.12 seconds; QRS 0.04 seconds.
Auricular rate 92; ventricular rate 92.
Small complexes. Slight left ventricular predominance. Occasional left ventricular ectopics. Slight tachycardia.

* Electrocardiogram by Dr. George R. Herrmann.

**Discussion.**—Some observers consider pernicious anemia to be a rare disease in the typical negro. This is not so in my own experience.* I believe it to be at least as common as in the white race. Ascites is said to occur with pernicious anemia, and probably small accumulations are common as part of the edema, so frequent in all severe anemias, but large collections of fluid in the peritoneal cavity, without accompanying edema, are rare. This man presents a large accumulation, and it was regarded, at first as merely part of the picture of pernicious anemia, but, though the blood rapidly became normal with the feeding of liver and liver extract, the ascites persisted and returned in just as large amounts following removal by paracentesis; the last tap was performed after the blood-picture was normal, yet the fluid returned just as promptly and injust as large amounts, varying in no way from the same phenomenon following the first tap, done when the anemia was at its worst. Palpation of the abdomen immediately after removal of fluid did not discover any masses, tumors, or enlarged organs. A pneumoperitoneum was attempted, but was unsuccessful. Cirrhosis of the liver seems to me to be the most satisfactory explanation of the persistent and recurring ascites; if this is the case it is interesting to speculate on the possible connection with the blood dyscrasia. Except for the presence of ascites, the general condition of the patient at the present time (December 22, 1928) is very good.

* Jamison, C.: Pernicious Anemia in the North American Negro, Southern Med. Jour., 19, 583–584, August 26th.

CLINIC OF DR. F. M. JOHNS

NEW ORLEANS, LA.

## AMEBIASIS, WITH SPECIAL REFERENCE TO ITS TREATMENT WITH IODO-OXY-QUINOLIN SULPHONIC ACID

NUMEROUS investigators have proved that the actual incidence of infection with the pathogenic *Endameba histolytica* is almost as great in northern climates as in the tropics, and yet the amebæ do not seem to be capable of localizing in sufficient numbers in the lower sigmoid or rectum to produce typical amebic dysentery. The reason for this is not apparent and has no parallel in other tropical protozoan diseases. Individuals from northern climates seem to be very susceptible to dysentery when in the tropics, and malaria when transported to the north gives a much higher percentage of successful inoculations than in a region where malaria is endemic. In the instance of malaria this has been explained on the grounds of an hereditary and acquired immunity to malaria, and it is only reasonable to presume that there should be a similar immunity to amebic infections. Amebic ulceration undoubtedly extends from the mucosal surface of the gut into the deeper layers, and it is quite possible that some degree of fairly constant irritation or injury to the rectal mucosa is a necessary contributing factor to produce this particular localization.

There is probably no disease the modern practitioner is called upon to treat that yields so spectacularly to treatment with such specific remedies as ipecac, emetin, emetin-bismuth-iodid, emetin combined with bismuth, or stovarsol as does amebiasis. All of these drugs have, however, exhibited at times, certain disadvantages either from the standpoint of difficulty in administration, toxicity, or ineffectiveness in establishing a permanent

cure. Within recent years it has been found that iodo-oxyquinolin sulphonic acid possesses unusual amebicidal properties and is said to be remarkably free from toxic effects upon the patient. It has been employed extensively by the German physicians under the trade name of Yatren, and it is manufactured in the United States by the Ernst Bischoff Company under the trade name of Anayodin. The use of this drug in several types of amebic infections may be illustrated by the following cases, which have been selected as typifying the usual range of severity in clinical symptoms that is to be met with in amebic infections. For brevity, only those symptoms pertinent to an amebic infection will be enumerated.

**Case I.**—Mr. B., white, aged thirty-seven years, was referred for diagnosis of a possible amebic infection by Dr. John B. Elliott, of New Orleans. The patient's history recounted numerous attacks of dysentery during the past few months, accompanied by the usual symptoms of abdominal pains, tenesmus, and the passage of bloody mucoid stools. There had been considerable loss in weight and he was practically incapacitated by general muscular weakness. There had been an average of ten to twelve stools per day for the week prior to examination.

The patient was requested to evacuate the bowels and the passage consisted almost entirely of mucus mixed with blood and was practically without fecal material. Numerous small grayish particles of necrotic material were noted, which, when fished out and examined, proved to be largely masses of amebæ, as many as several hundred to each 16 mm. field of the microscope being found. Under higher magnification the amebæ were found to possess large clear pseudopodia, barely visible nuclei and numerous phagocytized erythrocytes with an absence of ingested bacteria. The characteristic morphologic features of the amebæ, with the history of the patient, confirmed the diagnosis of infection with *Endameba histolytica*. Proctoscopic examination was not possible, the ulcerations apparently extending to and involving the internal sphincter.

*Treatment.*—Three grams of anayodin (four 0.25-gm. pills given three times daily before meals) were administered daily for a period of seven days. A rest of five days was allowed and another seven-day course of anayodin given.

By the third day of treatment all distressing symptoms had subsided and the number of stools dropped to three or four soft or watery fecal movements. There were no vegetative or encysted forms of amebæ found after this time. During the second course of anayodin the stools again became rather frequent, but the passages were without discomfort and did not contain blood, pus, or mucus. At the end of the second week the patient had gained sufficient strength to resume work as cashier of a bank.

Stool examination one month later showed a formed stool with no ab-

normal food remains and a careful search with centrifuge-concentrated specimens failed to reveal any encysted amebæ.

Another full course of fourteen days of anayodin therapy with a seven-day rest interval, was administered, following which monthly stool examinations for the past six months have failed to reveal any evidence of relapse. The patient has completely regained his original physical status.

**Case II.**—Mr. F., aged forty-six years, stationary engineer by occupation, was first referred to me three years ago for experimental treatment of amebic dysentery with stovarsol. At this time he had had recurrent attacks of dysentery for some years, in spite of treatment with ipecac pills, emetin, and bismuth. The presence of *Endameba histolytica* was determined in iron-alum-hematoxylin stained smears made from rectal ulcerations. Treatment with the routine daily dose of 2.25 gm. of stovarsol (acetyl-amino-hydroxy-phenyl arsenic acid) for fourteen days with a seven-day rest interval resulted in a clinical cure for two months, when dysentery recurred. Increasing the dosage of stovarsol to 3.5 gm. daily and repeating the seven-day course several times, a remission of three months was obtained. For the past two years he states that he has managed to stay at work by taking stovarsol in 3-gm. doses daily for a week out of each month. The stools have averaged three or four daily and are always soft to liquid and contain blood and mucus occasionally. Abdominal discomfort amounting at times to rather severe pains over the cecum has been rather constantly present.

The general condition of the patient was good. He was only a few pounds under weight, strength fair, and color good. A recently passed stool was semi-liquid, contained considerable mucus and numerous vegetative and precystic amebæ. There were only a few erythrocytes found. Proctoscopic examination showed a few small rectal ulcerations from which typical vegetative forms of *Endameba histolytica* were recovered.

Anayodin in 1-gm. doses three times daily for seven days was administered. Alternating with five-day rest periods, three more of the seven-day courses of treatment were given.

The abdominal discomfort was promptly relieved and it was noted that the stools became slightly more numerous and more liquid during the periods of medication. In the rest intervals bowel movements promptly returned to a formed consistency with a tendency to constipation. The patient has now been under observation for seven months, during which time numerous stool and proctoscopic examinations have failed to show any evidence of recurrence of the infection.

Another course of treatment identical with the first has been recently begun, as we know definitely that a relapse may occur many months after freedom from symptoms or demonstrable parasites in the feces.

**Case III.**—Mr. W., aged fifty-six years, a cotton broker by occupation. He was apparently in good health, although exhibiting a definite overweight. His complaint was a feeling of general lassitude, dull pains over the epigastrium, localizing occasionally in the right upper quadrant and he had noticed a slight daily elevation of temperature to 99° or 99.6° F. The liver was found to be definitely enlarged. *x*-Ray examination of the gastro-

intestinal tract was negative. The leukocyte count was normal and there was no pus found in the urine.

Examination of a hard formed stool showed an enormous number of cysts of *Endameba histolytica* each containing from one to four nuclei. These were definitely identified by wet-fixed and stained smears. No history of dysentery or loose bowels at any time for the past few years was obtainable; in fact the patient had found it necessary to take daily enemas to evacuate the bowels.

Treatment with anayodin, 1 gm. three times daily for ten days, followed by a five-day rest, and continuing with a seven-day course of medication, resulted in a return of the temperature to normal and disappearance of the abdominal discomfort. I was not able to demonstrate amebic cysts after the fourth day of treatment. Monthly examination of feces for the past fourteen months has failed to show any return of the infection. The liver is still enlarged, but there has been no temperature and the patient feels in the best of health.

It is interesting to note that a brother of this patient was operated upon for a liver abscess some fourteen months previously. The contents of this abscess were sterile, of a chocolate color, and amebæ were found in the drainage fluid on the third day following operation. There had been no dysentery preceding this abscess, and no vegetative or encysted amebæ were ever found in the stools.

**Case IV.**—Mr. J. K. D., a medical student, twenty-four years of age, apparently in good health, was found in the course of a routine class study to have numerous amebic cysts in his feces. These cysts were definitely identified as *Endameba histolytica*. He recalled having had an occasional attack of abdominal discomfort followed by a slight disturbance of the bowels for the past few months and which had been atttibuted to slight indiscretions in diet.

Treatment with anayodin, 1 gm. three times daily for seven days, followed by a five-day rest and continuing with another seven-day course of treatment resulted in prompt disappearance of the cysts. Frequent stool examinations during the past two years have failed to show any recurrence of the infection, together with complete freedom from intestinal disturbances.

## DISCUSSION

**Symptomatology.**—You are already familiar with the classical symptomatology of amebic dysentery, as shown by the first case presented, but I should like to call your attention particularly to the great variation, both as to the severity and as to the type of symptoms that may be exhibited in amebic infections in general. The symptoms in these patients have ranged all the way from a very debilitating disease produced by extremely extensive ulcerations of the colon with frank dysenteric symptoms, on through the milder types without dysentery, types such as

might easily be mistaken for other diseases of the gastro-intestinal tract, and finally to the apparently healthy, but infected, individual, whom we may class as the carrier.

It is interesting to note that with a localization of the lesions in the cecum and ascending colon, as shown by encysted amebæ found in the feces, there should be practically no dysentery but symptoms resembling a subacute appendicitis or cholecystitis. It is apparent also that definite ulcerations into the submucosa are present as shown by the symptoms of pain and elevation of temperature. I have encountered quite a number of cases of this type and have come to believe that every case presenting symptoms of chronic disease of the gastro-intestinal or biliary tract should be carefully examined for the presence or absence of amebic infection.

Numerous investigators have proved that the incidence of amebic infection is almost as great in northern climates as in the tropics, and yet amebic dysentery is almost unknown in the north. The reason for this is not apparent, and it has no parallel in other supposedly tropical protozoan diseases. Malaria, for instance, when inoculated into cases of paresis in far northern countries gives a higher percentage of high febrile reactions than the same strain of parasites will produce when inoculated into residents of a semi tropical climate. This has been explained on the grounds of hereditary and acquired immunity to malaria. It is only reasonable to presume a similar immunity to amebic infections. It is quite possible that this difference may be explained on the basis of the commonly recognized differences in diet and cooking between northern and southern countries which by altering the reaction, chemical constitution, or bacterial flora of the fecal residue would lower the resistance of the mucosa of the terminal portion of the colon by its contact between evacuations. Practically all dysenteric cases are accompanied by demonstrable ulceration of the terminal portion of the colon.

I have always regarded *Endameba histolytica* as practically an obligate tissue parasite, and as such it is difficult to conceive of a *healthy* ameba carrier. The fourth case presented comes as close to the conception of a healthy carrier as any I have been

able to find. It would appear that they all have from time to time some symptoms referable to actual tissue invasion of the colonic mucosa. It is very doubtful if pathogenic amebæ can live and reproduce to any extent or for any length of time in normal fecal contents.

All persons found infected with the pathogenic variety should be cured of their infection, for not only are such ameba carriers responsible for the spread of the disease, but those infected are themselves, at some subsequent time, apt to develop either dysentery or amebic liver abscess. I have in my records one such case; a patient that developed an abscess of the liver eight months following the demonstration of cysts of *Endameba histolytica* in his feces. Three months following the surgical drainage of the abscess the patient developed an acute amebic dysentery, and amebæ were found in the feces, as well as in the discharge from the abscess which had continued to suppurate and drain in spite of the efforts of the surgeon to sterilize the cavity.

**Diagnosis.**—A presumptive clinical diagnosis of amebic dysentery may be made and this confirmed by the finding of vegetative *Endameba histolytica* in the feces, but the diagnosis of the chronic, subacute, and carrier types of the infection is more apt to be made from routine stool examinations.

In the presence of dysentery, search should be made for the motile vegetative forms immediately after passage of the stool, or preferably in material scraped from the rectal ulcerations. Amebas are occasionally rather few in number, particularly in liquid stools, and with practice one may save considerable time and occasionally save a mistake in diagnosis by covering a comparatively large quantity of material with low magnifications.

In the use of the proctoscope, the fact should not be overlooked that often the lesions are limited to the rectum, and particular search should be made for small ulcers just above the sphincter.

In soft stools with precystic vegetative amebæ, these may be identified by wet-fixed smears stained with iron-alum-hematoxylin, or more easily by the characteristic cysts that will be

found after the administration of a few hypodermics of emetin. In the non-dysenteric patient, whether carrier or of the subacute type when examined in the interval between attacks of dysentery, the search should be directed toward demonstrating the presence or absence of encysted amebæ. For this I would recommend the study of unstained, centrifuge-concentrated specimens for the presence or absence of amebic cysts.[1] The centrifuge concentration and the washings of the specimen also permit one easily to see the cysts with the lower magnification of the microscope and thus to examine a large quantity of material. When found present the type of cysts should be identified by a study of unstained preparations for size, thickness of cyst wall, and presence of chromidial bars, and of preparations stained with Lugol's solution for enumeration of the number of nuclei and position of the karyosomes within the nuclei. A good detailed description of the various types of amebæ may be found in Dobell and O'Connor's manual, "The Intestinal Protozoa of Man."

**Treatment.**—All of these patients were treated experimentally with iodo-oxy-quinolin sulphonic acid administered orally. This drug was first used in wound infections, because of its high iodin content, where it exhibited a mild bactericidal property. Its early use in amebic dysentery was in the form of enemas, with the idea of promoting healing of the ulcers. It was soon found that the beneficial effect of the drug was probably due to its absorption and direct action through the blood-stream upon the amebæ invading the bowel wall, and that its action when administered orally was much more prompt and specific.

While all four of the cases here presented have been apparently cured, I have seen two patients who have relapsed following similar courses of treatment, one of whom received in addition daily enemas of 500 c.c. of a 1 per cent. solution of the drug. While not an infallible cure for amebic infections, anayodin certainly adds another valuable specific in the treatment of this disease and one that is apparently non-toxic.

The use of this drug was particularly advantageous in the second case here presented in that its use resulted in at least a

temporary cure of an infection that was definitely resistant to other forms of medication.

Treatment of amebic infection should be directed toward an eradication of the infection and with this end in view no matter what form of treatment may be employed the patient should be carefully examined at intervals for many months.

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## CLINIC OF DR. ISAAC IVAN LEMANN

NEW ORLEANS, LA.

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### OSTEITIS FIBROSA CYSTICA IN AN INFANTILE

THIS boy is sixteen years old. It is very evident at once that he is an infantile. Note his size. He has no evidence of secondary sexual characteristics (Fig. 205). His complaint upon admission was of smothering spells

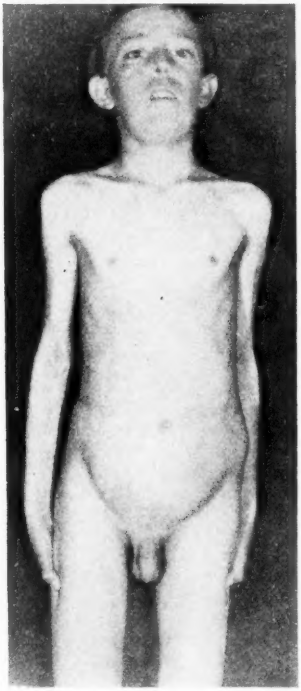

Fig. 205.—Front view of patient.

at night. Two months ago he fell down and bruised his left knee. He went then to his physician, who gave him a general examination and referred him to Dr. E. S. Hatch of our Orthopedic Staff. Dr. Hatch writes me as follows:

"I saw this patient on August 30, 1927, he being referred to me for consultation by Dr. W. A. Love. At that time he gave me the history that while going downstairs he slipped and fell, hitting his left knee. Local treatment did not help much. Patient states that the pain is worse at night and does not radiate. History of having fallen about eleven years ago striking his left tibia; since then parents have noticed that tibia began to enlarge and child has limped ever since.

"*Examination.*—Very thin, undernourished child, stands with both knees slightly flexed, feet in good shape except that anterior arches are relaxed. Teeth in fair condition; tonsils enlarged, but not reddened or inflamed; glands not palpable. Typical sabre tibia, both legs. Slight limitation of hip-joint motion probably due to abnormal shape of head of femur. Circumference left knee $10\frac{3}{4}$ inches; right, $10\frac{3}{8}$ inches.

"*Skiagraph* which was sent by Dr. Henriques shows marked osteoperiostitis of the right femur throughout its entire length even to the lower epiphysis. Same condition in left femur, but to a much less degree, also in both tibias and fibulas, the left tibia showing much more marked trouble than the right.

"My *diagnosis* was congenital lues plus traumatism of a diseased left knee-joint with synovitis. I advised absolute rest and mixed treatment. Since then I have not seen the patient."

A month from the date of the fall the patient was sent to our genito-urinary dispensary with the request that he be given salvarsan. The left knee was still swollen and stiff, slightly red and tender to touch. In the dispensary he received five doses of salvarsan (0.2 gm.) intravenously between October 4, 1927 and November 1, 1927. After two or three doses the swelling disappeared from his left knee and it was no longer stiff. At this time his ankles were not swollen and he was not short of breath. The day after his last dose of salvarsan he began to have smothering spells which he described as follows: "My chest was tight and I could hardly breathe. I would become short of breath, feel dizzy, and have a headache. I had never previously had any similar attacks." These smothering spells would last an hour or two, occurring once or twice a night but never in the daytime when he is about. Sitting up helps to relieve the attack. There has been no pain in the chest, merely a tight feeling with these smothering spells. At times he expectorates a small amount of mucus with the hacking cough he has. There has been no hemoptysis. Exertion easily causes dyspnea for the past week. His appetite is poor. Digestion is good. No nausea. No vomiting. He has a sour taste in his mouth. Bowels regular. Micturition: $\frac{1\text{–}2 \times N,}{3\text{–}4 \times D}$ no burning. His occupation requires him to be outside most of the time, exposed to the weather. He does not smoke.

*Past History.*—Other than measles and mumps and an injury at the age of five years, he has never been sick. He felt well up to the time of injuring the left knee two months ago.

*Family History.*—Father living, very nervous and has "rheumatism." His mother has been treated at another hospital for cerebrospinal syphilis,

and in this hospital for hysteria. Four sisters living and well. Two brothers living and well. All other members of his family are normal in size. A brother one year younger than the patient is a head taller than he.

*Physical examination* on admission showed a youth of an infantile type, undeveloped and undernourished, anemic, sitting up in bed, bright and alert.

Skin: Moist and elastic. Sallow anemic color to face. No jaundice of scleræ.

Eyes: No nystagmus, lacrimation, or photophobia. Pupils regular, reacted to light and accommodation.

Nose: No discharge. No gross abnormality. Ears: No discharge, hearing normal.

Teeth: In good condition. Throat: Negative. Tonsils: Not enlarged.

The nasal septum apparently destroyed by some process. Plugs of a dried greenish material present in nose.

The thyroid gland not palpable, posterior cervical chain of glands enlarged. No abnormal pulsations. No stiffness or rigidity.

Chest: Symmetrical. No lagging noticed. Respiration of a mixed thoracic and abdominal type. The superficial veins over chest fairly prominent.

Heart: Apex-beat is 6.5 cm. from midline in the fifth left intercostal space fairly well localized. No murmurs heard. Sounds good. Rate 66 and regular. No pulse deficit. Left border of heart 4 cm. from midline in third intercostal space Right border of heart at right border of sternum. Blood-pressure 155/90.

Lungs: Area of flatness over the lower part of the left lung; the upper border of which corresponds with the sixth dorsal vertebra posteriorly, the eighth rib in the postaxillary line and third intercostal space in anterior axillary line. Over the area of flatness tactile fremitus and breath sounds absent. Coarse crepitant rales heard over this area. On the right side resonance downward to a level with the eighth dorsal vertebra.

Abdomen: Somewhat distended, superficial veins marked. Liver not palpable but from percussion apparently three fingersbreadth below the costal margin. Spleen and kidneys not palpable.

Extremities: Pitting on pressure over ankles and legs. Tibias sabre shaped.

*Laboratory examinations* were as follows:

Urine: 1018 negative except for very few fine granular casts.

P. S. P.: First hour 52 per cent.
Second hour 12 per cent.
Total 64 per cent.

Blood: Red blood-cells 3,400,000.
White blood-cells 7900.
Polymorphonuclears 36 per cent.
Small mononuclears 6.
Large mononuclears 58.
Wassermann negative.

Sputum: No tubercle bacilli found.

Feces: Firm, yellow brown, negative.

The tentative diagnosis, therefore, based upon this history and physical examination is:

1. Infantilism unknown etiology.
2. Luetic bone disease.
3. Acute nephritis following administration of salvarsan.

We are at a loss, however, to understand the attacks of dyspnea. His account of them suggested rather a bronchial asthma than an asthma dependent upon his nephritis. His infantilism challenged our interest and attention as all such cases do. It is the generally accepted, though very vaguely understood, idea that infantilism represents some endocrine dystrophy. Many of the cases of infantilism have been associated with definite evidence of disease of the hypophysis. We observe neighborhood symptoms, such as headache, evidence of pressure upon the optic nerves producing constriction of the visual fields or even total blindness. Some, *x*-ray pictures of the skull show abnormalities of the sella turcica and I have in several cases seen dense shadows due apparently to calcification or tumor mass in the hypophysis itself. In other cases there have been no such clear indication of hypophyseal disease and writers have suggested a disturbance of the internal secretion of the thyroid or of the gonads. Even if we accept an endocrinopathy as the basis of the pathogenesis of infantilism, it remains always to find the etiologic factor of the endocrinopathy. This undoubtedly is not always the same. Sometimes, as I have already indicated, the cause is a neoplasm. In another place, in studying the type of infantilism of hookworm disease, I have suggested that this type of infantilism is produced by the deleterious action of the hookworm toxin upon the endocrine system. In the case of our present patient who seemed to have a bone disease and perforation of the nasal septum due to hereditary lues, we were inclined to interpret his infantilism as due to an endocrinopathy caused by lues. This assumption, however, was proved unwarranted in the light of further investigation.

We first looked for any other evidence of pituitary disease. Dr. H. N. Blum, oculist, reported the eye-grounds normal. The visual fields showed some concentric narrowing for color. Glucose tolerance tests were as follows:

100 gm. of glucose given

Blood

| | Mg. per 100 c.c. |
|---|---|
| Fasting specimen | 58.8 |
| ½ hour after meal | 95 |
| 1 hour after meal | 91 |
| 2 hours after meal | 68 |
| 3 hours after meal | 91 |

One week later: 100 gm. of glucose given.

| | Mg. per 100 c.c. |
|---|---|
| Fasting specimen | 76 |
| ½ hour after meal | 143 |
| 1 hour after meal | 110 |
| 2 hours after meal | 100 |
| 3 hours after meal | 100 |

The basal metabolic rate on three different occasions was: Minus 51.1 per cent., minus 37 per cent., and minus 26 per cent. Radiogram of the skull showed a normal sella turcica (Fig. 206).

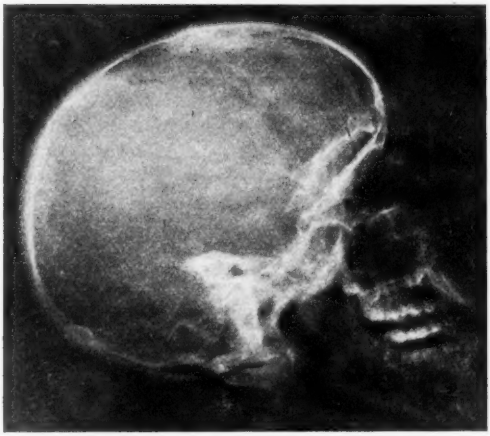

Fig. 206.—Skiagram of patient's skull showing normal sella turcica.

Fig. 207.—Skiagram showing retarded development.

We next turned our attention to the study of the skeleton with the idea of establishing the skeletal age. In this study we had the co-operation not only of Dr. W. F. Henderson, radiologist, but also of Dr. Isidore Cohn who

has made a special study of radiologic evidence of the development of the skeleton. Dr. Henderson reported that the radiograms of the long bones exhibited the osteal development of a child between ten and twelve years of age. He remarked that there were certain bone changes which were suggestive of lues but they did not warrant this conclusion absolutely. Dr. Isidore Cohn reported: "Examination of the available plates which are those of the shoulder (Fig. 207) and wrist (Fig. 208) suggests that the child is about ten years old from the point of view of the skeletal development. This partial conclusion is arrived at because of complete ossification of the pisiform bone, the absence of the acromion apophysis and the wide epiphyseal line at the upper end of the humerus. I suggest pictures of the ankle, elbow, and hip as I believe conclusive evidence will be obtained from the presence or absence of the epiphysis of the olecranon, of the epiphysis of the os calcis, and of the epiphysis of the lesser trochanter." When these further skiagrams were taken in compliance with Dr. Cohn's advice, Dr. Henderson reported:

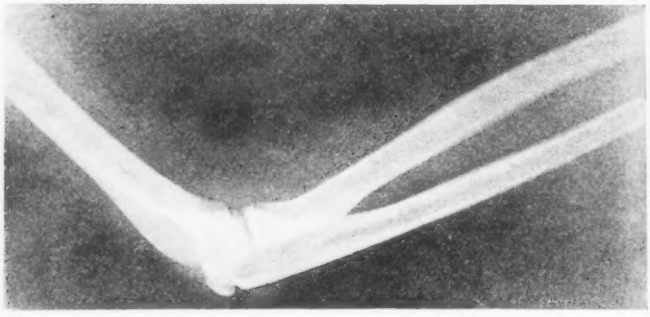

Fig. 208.—Skiagram showing retarded development.

"All the bones of the pelvis, lower extremities (Fig. 209) and elbow region (Fig. 210) show the status of development of the skeleton to be eleven years of age. The ilium has not yet fused with the ischium, the lesser trochanters are still free as is the olecranon process. A point of unusual interest observed in the left femur is a very extensive involvement in which the cortex is both expanded and thinned down with large cyst-like bodies observed in the medullary canal (Fig. 210). Perpendicular striations are visible in the bone but no production has occurred beyond the periosteum. The changes are typically those seen in osteitis fibrosa cystica."

Meanwhile Dr. H. L. Kearney had reported: "There is a perforation of the septum involving only the quadrangular cartilage—the bony septum is not affected. This could be from lues but there is usually bone involvement in lues and a diagnosis of lues from the lesion alone is not warranted."

With these reports before us, we were confronted with a set of facts which permitted, if indeed it did not demand, an inter-

pretation other than that based upon the assumption of hereditary syphilis. The type of bone lesions shown by the *x*-ray and particularly the finding of osteitis fibrosa cystica were not good evidence for congenital lues. Osteitis fibrosa cystica was first described by von Recklinghausen.[1] Hirschberg[2] is said to have given a description of the disease, but did not recognize it as a separate entity, considering it a form of osteomalacia. Von Reck-

Fig. 209.—Skiagram showing retarded development.

linghausen described the disease which has since borne his name as occurring usually in young adults. Its course is chronic and the clinical picture presents few symptoms other than vague, though at times quite severe, pains and frequency of spontaneous fracture. "As the disease develops a tissue of fibrillar character appears in the bones, the marrow is changed into connective

Fig. 210.—Skiagram showing retarded development, also the osteitis fibrosa cystica in the left femur.

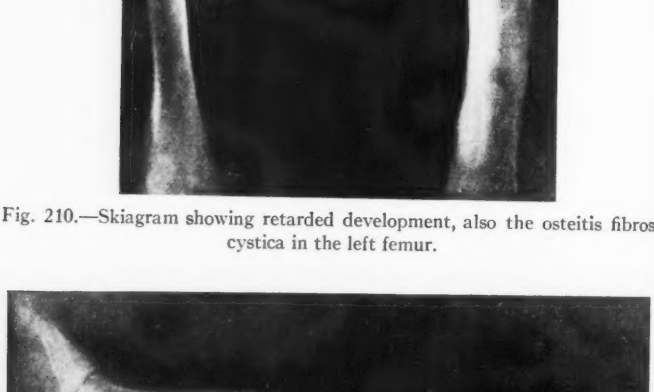

Fig. 211.—Skiagram showing retarded development.

tissue, bone substance is resorbed and cysts, often large, are found. Side by side with this retrogressive change a progressive process takes place with new growth of bone or osteoid tissue and quite often proliferation of cells so vivid that the tissue produced may easily be mistaken for a giant-cell sarcoma."[3] The special points to be noted are the fibrous transformation of the bone-marrow with formation of new bone, and the early rarefaction of the cortex which may be reduced to a thin shell of bone or entirely replaced by fibrous tissue. These changes may occur in a single bone or may affect many bones of the skeleton. Von Recklinghausen considered that most benign bone cysts were due to this osteitis fibrosa, the solitary cysts being caused by a localized form of the disease. There has been considerable discussion in the literature as to whether solitary bone cysts represent a separate entity from the generalized form, but no one has established any good ground for believing this.

In 1877 Paget[4] "described a chronic inflammation of bone occurring in people past middle age; the disease usually affects several bones, and is accompanied by a peculiar thickening, softening, and bending of the bones, which result in a characteristic clinical picture in which spontaneous fracture is rare. The pathologic changes in the bones show: (1) An extensive resorption of bone by osteoclasts; (2) an excessive new formation of bone, laid down by osteoblasts on the resorbed surface of the old bone, so that the cortex which had become rarefied may become dense, especially in the skull; (3) the bone-marrow becomes transformed into fibrous tissue and encroaches on the cortex, and in this fibrous tissue osteoid bone is laid down, the lamellæ of which run in every direction; (4) subperiosteal layers of bone are formed which add to the volume of the bone in thickness; (5) occasionally cysts or spaces filled with fluid are present in the fibrous tissue and occasionally tumor-like tissue with numerous giant-cells. The special points to be noted in this description are the fibrous transformation of the bone-marrow with formation of new bone, and the early rarefaction of the cortex which later may become dense with irregular Haversian canals; the new bone both in the medulla and the cortex is at

first osteoid but may become calcified so that the bone regains its rigidity."

There have been many suggestions that the two diseases—Paget's osteitis deformans and von Recklinghausen's osteitis fibrose oder deformirende (osteitis fibrosa solida or cystica)—are different forms of the same disease. The original conception was that von Recklinghausen's disease attacks children and young adults while Paget considered his disease one of mature life. "Seth Hirsch, Sikes, Packard, Stelle, and Kirkbride found in the study of 51 cases, the average age to be forty-nine and a half years."[16] The changes of osteitis fibrosa cystica have been found even in the early weeks of life. Ireland[17] reported the youngest case on record—a child forty days' old. I. Seth Hirsch[16] believes that the disease is probably congenital with strong hereditary tendencies.

Cysts are frequent in osteitis fibrosa and relatively rare in osteitis deformans, although they do occur in the latter disease. Many have pointed out that the histologic pictures present transitional forms between the two diseases. While it cannot be said that they are surely identical, there is considerable evidence suggesting this. Thus Eising[6]: "Although osteitis deformans and osteitis fibrosa present decided clinical differences, upon histologic analysis, these differences are more in quantitative ratio than in fact." There is neither time nor purpose to elaborate here upon this point. I wish merely to indicate that there is probably underlying these two diseases, and probably also the single bone cysts, the benign giant-cell tumors, and similar bone diseases, a fundamental constitutional depravity. I do not mean by this that the basic condition is necessarily the same in all of the bone dystrophies. As Landon[7] points out, no sharp distinction can be made between osteitis fibrosa and the solitary cysts. The solitary cyst is limited to *one* bone in which the cyst formation is the prominent change, while in general osteitis fibrosa cyst formation is of minor importance. The essential underlying process leading to the production of cysts is osteitis fibrosa of the type limited to a part or whole of a single bone.

Both von Recklinghausen and Paget originally regarded the

bone diseases described by them as essentially inflammatory in origin. In 1910 von Recklinghausen[8] included it in a group of metaplastic malacias, regarding it as an anomaly of metabolism. Bloodgood[9] and others have also regarded osteitis fibrosa cystica as inflammatory. No one, however, has been able to bring evidence in support of this position and in recent literature this view has been abandoned. Another theory is that the disturbance of bone metabolism has been due to improper diet; in other words that we are treating a deficiency disease. E. P. Corson White[14] in a study of 3 cases of osteitis deformans in monkeys thought that the bone changes might be just one stage in a deficiency disease. They might be a "reparative response; first, through a distorted neurotrophic mechanism; second through the perversion of calcium governing glands which have been distorted by an improperly balanced diet or, third, through the addition of an excess of calcium to the diet of an animal whose body fluids were unable, through previous faulty diet or other disorders, to hold it in solution." The bone pathology in his cases included cysts and White comments that the picture was very like osteitis fibrosa cystica. White refers to reports by others of similar bone diseases in horses, goats, monkeys, and a young lion. All communications referred to domesticated animals or to animals in captivity. All of them, therefore, were living under unnatural conditions, perhaps in-cluding conditions of improper diet.

There are many references in the literature to the theory of an endocrinopathy as the underlying cause of these bone dystrophies. White for example goes on to say: "Da Costa[15] believes the disease to be a disorder of bone metabolism probably dependent on the absence or perversion of some internal secretion. There is much evidence on hand to prove that disorders of the ductless glands do influence bone metabolism, and changes in these glands have been reported in cases of Paget's disease, although the findings and lesions have been far from uniform or distinctve, and have not been confined to one gland. Eight cases were reported as possibly being hypothyroid conditions; pituitary changes were found in 3, suprarenal changes in 1; parathyroid reported missing

in 2; 3 had sclerotic thyroids. Many reports make no mention whatever of the glands of internal secretion.

"Da Costa interprets the retention of calcium, phosphorus, and magnesium, with the sulphur loss found in these cases, as indicating a stimulated osseous or osteoid formation, accompanying the resorption of a highly sulphurized organic matrix. In the course of this calcification procedure, he supposes that a certain quota of the sulphur of the matrix is replaced by other elements, a process which must entail retention of calcium, phosphorus, and magnesium, and increased elimination of sulphur. He shows the close parallelism between the mineral metabolism of a growing boy, a case after parathyroidectomy, and a case of osteitis deformans, and suggests that this depends in some way, either on the absence or on the perversion of some internal secretion, possibly the parathyroids, which controls calcium exchange in the body. From some cause, substances arise which have the power to abstract calcium from the body tissues, the abstraction of these salts being the first step in the production of the disease. This theory of Da Costa's most satisfactorily describes the history of the monkeys which we wish to report."

The rôle of the parathyroid in regulating calcium metabolism has been made clearer in recent years since the isolation of its hormone by Collip. A suggestive point is that there are in the literature a number of reports of osteitis fibrosa cystica associated with parathyroid tumors. Such are the cases of Gold,[10] Gödel,[11] Meyer,[12] and Dawson and Struthers.[5] Meyer cites similar findings of Schmorl, Erdheim, Askanazy, Strada, and Bower. In our present patient we have found no evidence of parathyroid tumor. His blood-serum calcium was 11.2 mg. per 100 c.c.—a perfectly normal finding. Liles and I[13] have pointed out elsewhere in connection with the loss of bones in leprosy that gradual resorption of bone tissue is not accompanied by any disturbance of the blood-serum calcium level nor was such disturbance to be expected in view of the physiologic regulatory mechanism. To have more definite information upon this point, it would be necessary to study the calcium phosphorus magnesium sulphur balance as White did in his monkeys.

It has seemed worth while to put this additional case of osteitis fibrosa cystica on record because its occurrence in an infantile would seem to lend additional weight to the belief of an underlying disturbance of the endocrine apparatus. We are not in a position to say which endocrine organ is at fault in our patient.

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## BRONCHIAL POLYP ASSOCIATED WITH MEDIASTINAL MASS (PROBABLY MEDIASTINAL LYMPH-NODES); THE LATTER CAUSING THE PRESENTING SYMPTOM OF DYSPHAGIA

I PRESENT this patient because her case illustrates the very great advantages of modern roentgenologic, endobronchial, and endo-esophageal diagnostic methods. It represents, unfortunately, however, also our inability to come to a satisfactory conclusion concerning a mediastinal mass in spite of the information furnished by these modern methods.

Mrs. J. G. A. aged thirty-six years came to consult me in August, 1927. One month previously she had pain in the region of the sternum when she swallowed. There were stages of the pain as the food went down. This lasted about a week. Her doctor gave her a prescription which caused nausea if she ate immediately thereafter. The pain was relieved and she had no more trouble until August 7th, when during the night she became aware of a "lump behind the sternum and through to the back between the shoulder blades." This sensation of a lump persisted. At times since August 7th she had momentary pains which came in waves. There was no relation to food. Her appetite was ordinarily good, but she had none since August 7th. She had lost 6 pounds in two days. She took almost no food on August 9th and had taken two laxatives (cascara and milk of magnesia) since August 5th, which caused a number of bowel movements. The bowels were ordinarily inclined to constipation, but she usually did not take a laxative for she had a bowel movement almost every day. No sour stomach. No heart burn. Slight belching. "Phlegm" kept coming into her throat. No cough. No dyspnea. At times when she lay down, she had pounding of the heart. Slept well. Headache formerly but none in the past year or so. She was better in this respect since her treatment by Dr. Weil for sinus trouble. Micturition: $\frac{O \times N}{4\text{-}5 \times D}$ Menses: None since the birth of the baby ten months old.

*Past History.*—Measles, whooping-cough, and chickenpox in childhood. Influenza slight in 1920. Sinus trouble in 1924—treated by Dr. Weil, no operation—pregnant at that time. Kicked over the right eye at the age of six; "a bone was pushed backward into the brain." Eight children, all living and well. No miscarriage.

*Family History.*—Father died, aged sixty-four, carcinoma of the frontal sinus. Mother died, aged fifty, cause unknown. Patient was the only child. Husband living and well.

*Physical Examination*—Healthy looking, obese woman. Weight 178¾ pounds. Height 5 feet, 7½ inches. Skin: Normal. No adenopathy.

Mucous membranes: Normal. Throat: Negative. Tongue: Somewhat coated. Neck: Negative.

Thorax: 97 cm., 102 cm. full inspiration, 75 cm. full expiration. No tenderness on percussion over the sternum.

Lungs: Normal.

Heart: Rate 88 sitting. Blood-pressure 126/70.

Dulness fifth left intercostal space 8 cm. from the midline.

Dulness third right intercostal space 1 cm. from the midline.

No murmur. No irregularity.

Abdomen: Relaxed, tenderness in the right hypochondrium. Liver and spleen not felt.

Knee-jerks: Normal.

Scar over the frontal eminence on the right side. Suggestion of external strabismus of the right eye.

Pupils: Equal, regular, symmetrical, react to light and accommodation.

*Fluoroscopic Examination.*—Heart: Normal.

Aorta: Normal. In the posterior mediastinum an indefinite shadow about halfway down.

Lungs: Normal.

*Laboratory reports:*

Urine: A. M. 1022 acid yellow turbid albumen trace, sugar 0, indican 0.
P. M. 1024 acid yellow turbid albumen heavy trace, sugar 0, indican 0. Aldehyd 0.

Sediment: Pus large amount, mucus, ep. cells, urates.

Blood: Wassermann negative.

Hemoglobin 85 per cent. No abnormal cells found in smears.

Thinking perhaps that her troubles were due to gall-bladder disease I sent her to Dr. W. F. Henderson with the request that he try to obtain a visualization of the gall-bladder after the administration of dye. He reported as follows:

"Following the administration of the opaque dye, the gall-bladder shadow is observed to begin filling upon plate No. 1; plates No. 2 and 3 show an increase in filling and concentration, while plate No. 4 shows a satisfactory emptying and the evidence here obtained is insufficient to condemn this gall-bladder. At fluoroscopic examination of the chest, the cardiac shadow appears to be normal in size but the great vessels are somewhat widened, particularly just above the heart. In the lateral projection the aorta appears to be somewhat wider than normal. The administration of the barium capsule shows this to come to rest in the posterior mediastinum (Fig. 212), behind the upper margin of the heart, remaining at this location over a considerable period of time. Following the administration of four doses of atropin the procedure is repeated. Again the barium capsule comes to rest in the identical location. As the capsule breaks up and the barium proceeds slowly through the constricted portion of the esophagus, the esophageal wall does not present the cauliflower-like projections and irregularities of its margins which are so commonly seen in malignancy, and it is impos-

sible to conclude that malignancy is existing. The failure of atropin to relax this is considered evidence of its true rather than reflex nature, which is subsequently borne out by the fact that an anesthetic administered for the purpose of esophagoscopy likewise fails to relax the constriction."

The patient was then admitted to Touro Infirmary for an esophagoscopy. This was done by Dr. A. I. Weil, who reported:

"Esophagoscopy performed under general anesthesia. The tube passed easily about halfway down the esophagus and there it seemed to come on an

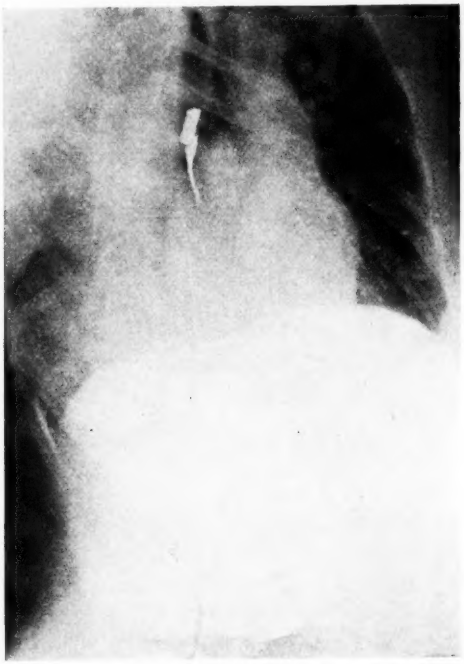

Fig. 212.—Lateral view of chest, August, 1927. Two barium capsules lodged in esophagus. Just to the right of the lower capsule there is seen in the posterior mediastinum the mass to which reference is made.

obstruction, which prevented the tube from going further in. This closure seemed quite tight but there was no sign of polypoid growth or other indication of esophageal carcinoma which could be made out through the esophagoscope, other than the obstruction."

In spite of the absence of a definite finding of a carcinoma intra-esophageally and in spite of the extremely well nourished condition of the patient, Dr.

Weil and I felt that we were dealing with an organic and not a functional obstruction and in all probability this obstruction was due to some malignancy in the mediastinum.

She then went home but returned in about a month saying that she had not been able to eat any hard food. She took only liquids and soft cereals. She felt weak but had actually gained weight. On this second visit, Dr. Weil and Dr. H. L. Kearney did an esophagoscopy again, September 16, 1927, and reported:

"Nine mm. full lumen Jackson-Mosher esophagoscope passed into stomach without encountering any evidence of esophageal obstruction. Inasmuch as the fluoroscopic examination had found evidence of esophageal obstruction

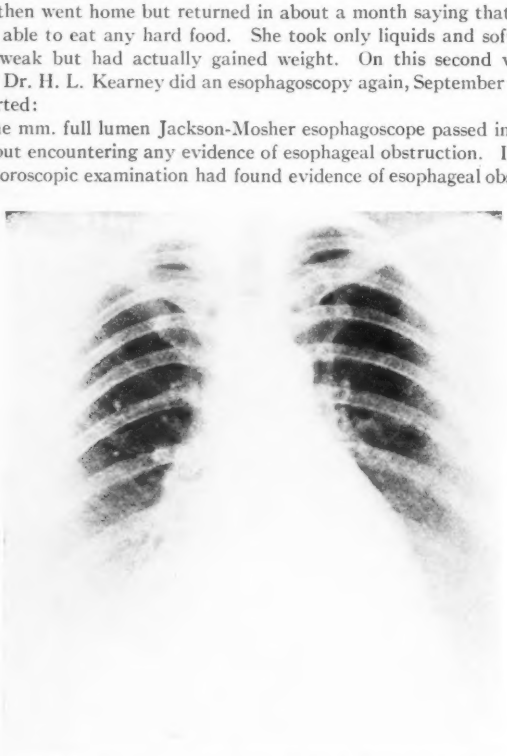

Fig. 213.—Anteroposterior view of chest, August 11, 1927.

at about the level of the crossing of left bronchus, this neighborhood was very carefully examined for pathology or pressure. There was no evidence of encroachment on the esophageal lumen either by endo-esophageal pathology or by pressure from some external structure. On the anterior esophageal wall, 26 cm. from the upper incisor teeth was encountered an area of mucosa about 8 mm. in diameter which did not look normal; there seemed to be some slight thickening in this area."

She went on a full diet at the end of the week when the soreness of her throat had subsided. She ate with relish and without difficulty until October 8th when after eating peanuts she experienced the same kind of pain behind the sternum that she had originally had, only less intense.

The pain lasted only a day or two. It was very slight and came in paroxysms. She continued to eat solid food without trouble and when she was seen on October 12th she declared she felt strong and well and her weight was 181 pounds. On October 25th she returned. The slight retrosternal discomfort continued until October 17th when it became considerably worse. She then began to cough and to bring up foul-smelling gas. In spite of all her suffering her appetite had remained good and she enjoyed her food. There was no pain over the sternum following eating but a slight pain between the scapula fifteen minutes after eating. On November 1st, she wrote: "The pain between the shoulders continues every day at intervals. The foul

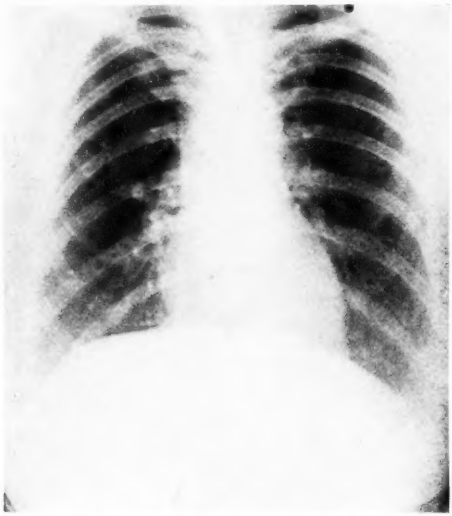

Fig. 214.—Anteroposterior view October 15, 1928 showing lung fields clear. There is no evidence of neoplasm of the lung.

odor still bothers me. The hacking cough is worse. The entire chest is sore from it." An *x*-ray of the chest on November 5th was reported on as follows:

"The administration of a fluid medium shows the barium to pass without difficulty through the esophagus. It is likewise true that at the administration of a capsule at this time it appears to pass quite freely through the esophagus. In the anteroposterior position, no masses can be observed in the chest but in the true lateral position, an oval mass the size of an egg can be observed behind the great vessel shadows, and opposite the third, fourth, fifth, and sixth dorsal vertebræ."

On November 7th she was subjected to a bronchoscopy because of a cough and the story of a foul odor. Dr. Kearney reported: "Bronchoscopy with the 7 mm. Jackson aspirating bronchoscope showed a moderate amount of

bronchial secretion coming from the tracheobronchial tree. Examination of the orifices of the bronchi to the various lobes of the lung reveals no pathologic secretion coming from any lobe. Bronchial motility normal on both sides. There is no widening of the carina and it moves downward and forward normally during deep inspiration. On entering the right bronchus a smooth rather firm pedunculated nodule about the size of a pea was found springing from the antero-internal wall probably about 2 cm. beyond the carina. The nodule was slightly paler than the bronchial mucosa and obstructed about one-half of the bronchial lumen. The mass was removed in its entirety with specimen

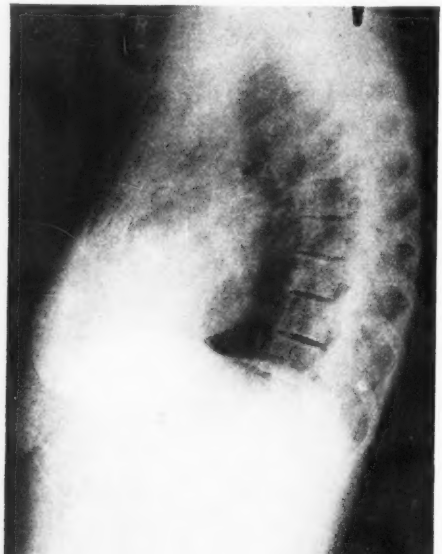

Fig. 215.—Lateral view October 15, 1928 showing the mass still present. It is as large as ever, but apparently not as dense.

forceps, leaving a smooth bronchial wall and unobstructed bronchus. There was very slight bleeding. Clinically the tumor appeared to be benign."

The tissue from the bronchus was reported on by Dr. J. A. Lanford, pathologist, as follows: "The tissue is a polypoid-like structure made up of supportive tissue containing blood vessels and showing a number of lymphoid and plasma cells scattered throughout, they being particularly striking around the blood-vessels. The surface is covered with stratified squamous epithelium, which is adult in type, with the

exception of a small area of ulceration and the attachment to the underlying part. No evidence of new growth or malignancy found. Diagnosis: Polypus showing chronic inflammatory reaction."

She was then readmitted on November 29th for another bronchoscopy. Dr. Kearney reported: "Bronchoscopy was done with the 7 mm. Jackson aspirating bronchoscope. There was no more than the normal amount of tracheobronchial secretion. There was no broadening, nor interference of the motility of the carina. About 2 or 3 cm. beyond the carina was found a tumor mass springing from the antero-internal wall of the right main bronchus and obstructing about one-half of the bronchial lumen. There was no infiltration of the bronchus and bronchial motility at this point was normal. It was not possible to see beyond the tumor but there was no pus coming from below. This mass has recurred since the previous admission of this patient about three weeks ago and if it continues its rate of growth, the middle and inferior lobe of right lung will be obstructed. There was no bleeding on manipulation of the tumor. Twenty c.c. of lipiodol was introduced into the middle and inferior lobe of right lung beyond the tumor mass."

December 15, 1927: After the bronchoscopy she had, for a while, the feeling of food being lodged behind the sternum. This became worse up to about December 8th, but since then she has not had it at all. It disappeared suddenly. The bad odor continued until December 12th. The appetite had been good up to a few days previously. Physical examination showed nothing abnormal in the chest except that the inspiratory murmur was a little more intense in the right interscapular space than in the left. Heart: Normal, blood-pressure 120/70. Another bronchoscopy was done by Dr. Kearney December 15, 1927, who reported:

"Bronchoscopy was done with the 7-mm. Jackson aspirating bronchoscope. There was little excess of bronchial secretion coming from below the bronchial tumor mass—which was located in the right main bronchus about a couple of centimeters beyond the carina. Specimen of the tissue of the mass was removed for microscopic study but the entire mass was not removed. The bronchial motility was normal. There was no infiltration of the bronchial wall. The mass does not bleed readily and is clinically a polypus."

*Laboratory Report* (Dr. J. A. Lanford).—"Specimen is a small piece of tissue about ½ cm. in diameter, soft but cellular in character and bright pink in color. Organizing exudate—no distinct neoplasm. Apparently granulation tissue."

On December 20th there was some return of the bad breath. This continued until January 1st but there has been none since. Occasional slight hurting behind the sternum. Appetite good. She had gained some weight and looked fine. A day or so after the last bronchoscopy she coughed up some small pieces, apparently of the tumor. On January 18th she spat up several mouthfuls of blood after coughing. In January she developed trouble in her left antrum of Highmore for which she was treated by Dr. Weil. The cough had continued until April. On April 1st and again on the third she spat blood. On the latter date she coughed up a little mass about the size of a large pea. She continued to spit blood for the rest of the day. On

April 4th the sputum was still stained with blood. On April 12th she brought with her in a little vial the polyp which she had spat up. Dr. Lanford reported on this as follows:

"Examination of the tissue shows it to be a polypus which just above its attachment is covered with a few epithelial cells, some of which are ciliated, but for the most part the surface is free of epithelium. The polypus is made up largely of blood-vessels, very loose connective tissue and inflammatory reaction, both acute exudative and chronic proliferative. It gives a picture of granulation tissue and nowhere is there any suggestion of a malignant neoplasm."

She had had no retrosternal pain except in February and again on April 3d. She looked fine. Physical examination revealed nothing of importance.

July 9, 1928: Except for a cough she did very well until the first week in June when she had abdominal pain and loose bowels for a few days. Following this she lost her appetite and has not recovered it. About June 18th she began having retrosternal and interscapular pain after swallowing. Because of this she took only soft food for two or three days and as this did not make the pain any better she went on a diet of malted milk only. The pain then stopped and when she resumed eating it did not return. She still had a sensation of a lump or soft rubber ball retrosternally or retromanubrially. Slight cough, but no odor to the breath now. She did have an odor to the breath with the cough the middle of June. Although she thought she had been losing considerable weight since about the middle of June, she still weighed 183 pounds. Physical examination revealed nothing of importance. *x*-Ray report July 9th was as follows:

"In the anteroposterior position, the diaphragms, heart, and aorta appear to be normal and while the structures at the hilum are somewhat wide, they are not otherwise characterized by evidence of pathology. In the lateral projection the chest appears to be normal with the exception of the shadow which was previously observed in the posterior mediastinum and is still exhibited as a large oval mass behind the aorta and auricular region of the heart. This shadow is still smooth but appears to be considerably larger than at the previous examination. The shadow can be likened to the size of a very large gall-bladder."

July 11, 1928: "Bronchoscopy was done with the 7 mm. Jackson aspirating bronchoscope and revealed a stenosis of the right bronchus, about an inch beyond the bifurcation. This was apparently due to an encroachment on the lumen by thickening of the bronchial wall on the left side at the site of the polypus, which was removed last year. Bronchial motility at this point was normal. There was no infiltration suggestive of malignancy. Esophagoscopy was done with the 9-mm. Jackson full lumen esophagoscope, stomach was entered without difficulty. The area previously noted 26 cm. from the incisor teeth did not display any evidence of pathology."

On August 4th she still had difficulty in swallowing at times and the heaviness behind the sternum. She had no appetite and was not eating well, but in spite of this was working twelve hours a day. She felt that she had

no strength due to lack of food. This time she weighed only 170 pounds, a loss of 13 pounds in a month. The blood-picture was as follows:

| | |
|---|---|
| Hemoglobin | 75 per cent. |
| Red blood-cells | 4,240,000 |
| White blood-cells | 5750 |
| Polymorphonuclears | 58 |
| Large mononuclears | 5 |
| Small mononuclears | 34 |
| Eosinophils | 3 |

From August 7th to October 17th she has received six treatments with deep *x*-rays.

October 11th she comes now because she has noticed a little bleeding from the vagina from time to time when she stands a good deal. Dr. Walter Levy proposes to cauterize the cervix under gas anesthesia. He says that the trouble is due to a laceration and endocervicitis. The patient weighs only 160 pounds, a loss of 23 pounds since June. The loss of weight is very apparent. She says that she has had no bad breath for many months. The sensation of the lump in her chest she has only rarely. She has a very slight cough occasionally. Once while romping she had a pain in the chest. She continues to work hard and is on her feet many hours during the day. Physical examination shows nothing new. Fluoroscopic examination: The mass, if altered at all, is smaller. *x*-Ray report October 15th was as follows:

"No alterations can be observed in the diaphragms, the heart, or aorta. The pulmonary fields give no evidence of infiltration or coalescing densities. In the lateral projection there is still to be observed a fairly large oval shadow previously seen and it cannot be stated that this has changed particularly in size."

How are we to interpret the findings here? Of two or three things we are quite certain. She had an endobronchial polyp. She had and still has a large mass in the mediastinum pressing upon her esophagus and at times preventing the prompt entrance of food into the stomach. This has caused the retrosternal and interscapular pain. The cough and foul breath were undoubtedly due to the endobronchial polyp. Are we to assume that the endobronchial polyp and the mediastinal mass have no relation one to the other? I find it difficult to make this assumption. Endobronchial polyps, while not a rarity, are not an every day occurrence. Mediastinal masses, such as this, are also unusual. It is difficult to believe that one patient should have at the same time two such unusual findings without their being related. If on the other hand we try to think of some relation between the two, we are equally put to it. In the first place we must try to form a clear idea as to the structures involved in the mediastinal mass as well as its probable nature. The mass is not an aneurysm nor is it related to any of the vascular structures. We can think of only one structure in this location to which it can with reason be referred; namely, the mediastinal lymph-nodes. If the mass represents a conglomeration of enlarged lymph-nodes, we may consider three or four possibilities. In the first place it might be a metastasis of malignant disease elsewhere. This seems untenable, as we have not discovered any primary

new growth, and after the lapse of a year a new growth which had metastasized to the mediastinum would have certainly itself become evident and would have by this time made the patient cachectic. This she is not. Secondly we may think of the lymph-nodes being enlarged in the course of some blood dyscrasia. This hypothesis is negatived at once by the result of the blood examination. Thirdly, the lymph-nodes may be the site of tuberculosis. This cannot be regarded as probable in the absence of any evidence of tuberculosis in the lungs. Fourthly, the lymph-nodes may be enlarged as the result of syphilis. This cannot be regarded as probable as there is no other evidence

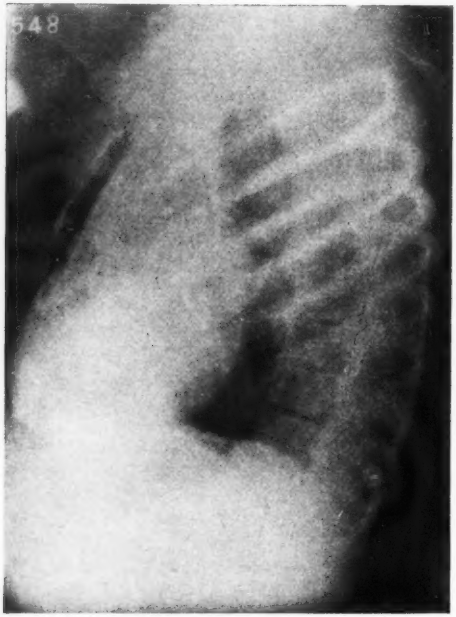

Fig. 215*a*.—Lateral view of chest, December 16, 1928, showing complete disappearance of the mass in the posterior mediastinum.

in the physical examination and history or the Wassermann reaction of the patient. Finally, the lymph-nodes in the mediastinum may be enlarged as the result of infection of the polyp in the bronchus and the subsequent drainage to the lymph-nodes. This by exclusion seems to be the most plausible explanation and it is the one that we have adopted as the tentative and working diagnosis. I confess that it is open to objection—first that the mass is unusually large for lymph-nodes and second that with the removal of the polyp there should have been some recession of the glandular infection and enlargement.

At the beginning of November, 1928, the patient had a cough and spat bloody mucus and finally coughed up another small polyp. After a few more days and immediately after a coughing spell she felt something hard in the back of her throat "where the nose joins the throat." She brought up then a little piece of hard, almost bone-like, material about ½ cm. in diameter. After this she ceased coughing.

On December 14, 1928 she weighed 154 pounds, reported that she was working as hard or harder than ever, and had plenty of energy. A skiagram of the chest at this time showed that the large mass in the posterior mediastinum had disappeared entirely. The barium capsule passed without difficulty into the stomach instead of coming to rest opposite the shadow of the mass as formerly.

**Summary.**—Patient is presented who had complained primarily of retrosternal pain which was proved by fluoroscopy and roentgenologic examination to be due to a mass in the mediastinum. Because of the negative findings on esophagoscopic examination and because of the development of cough and foul breath the bronchoscopic examination was made and revealed a polyp. The possible relation of the polyp to the mass in the mediastinum was discussed and it was suggested that the mass represents an agglomeration of lymph-nodes infected from the polyp.

CLINIC OF DR. RANDOLPH LYONS

NEW ORLEANS, LA.

# REPORT OF A CASE OF ARTERIOSCLEROSIS, MYOCARDITIS, PULSUS ALTERNANS, AND POSSIBLE CORONARY OCCLUSION, WITH SOME OBSERVATIONS UPON THE VALUE OF CERTAIN OF THE NEWER DIURETICS IN CARDIAC EDEMA*

MY object, gentlemen, in presenting to you today the history of this patient is twofold. In the first place the case was under close observation for almost two years and presents certain features of unusual interest. Second, the patient was particularly well adapted to study the effects of diuretics in a certain type of heart disease. The patient ultimately died, and unfortunately, autopsy was not permitted.

Mr. J. L., 60 years, night watchman, widower, admitted to Touro Infirmary June 6, 1925. Discharged June 27, 1925.

Diagnosis: Chronic myocarditis. Cardiac dilatation. Coronary thrombosis (pericarditis). Arteriosclerosis.

Complaint: Shortness of breath.

Present illness: Has not been feeling fit for about six weeks. Has not been able to do as much work as usual, even though his work is not hard. Tires easily. Four days ago began to suffer with shortness of breath, at first only after exertion but for past two days almost constantly. Has been unable to lie down flat in bed or sleep for three nights. Has suffered no pain but has occasional dizzy spells. His vision has not been so good during last week. Rarely has headaches. Very little swelling of feet. No urinary disturbance. Digestion good. Bowels moderately costive. Has had a nonproductive cough for past four days.

*Past History.*—Typhoid many years ago. Several mild neisserian infections in younger days. Denies lues. Was told by a doctor five or six years ago that he had high blood-pressure.

*Family History.*—Father died of Bright's disease. Family history otherwise negative.

*Clinic delivered before the Graduate School of Medicine, Tulane University.

*Physical Examination.*—A small, white man, well developed, and fairly well nourished. He is orthopneic and cyanotic. He appears restless but complains of no pain. Temperature 101° F.; pulse 130, regular; respiration rapid. Slight edema of ankles and feet. Moist râles audible at both bases. Heart is enlarged slightly to the right but chiefly to the left where it extends to the anterior axillary line in the sixth intercostal space. At the apex the first sound is distant and muffled, the second sound is louder. At the junction of the fifth rib and left sternal border is heard a to-and-fro murmur; the sounds are creaking and leathery in character and quite loud. This rub is present when the breath is held (patient complains of no pain). Liver border is palpable. Blood-pressure 135/95.

Urine: Specific gravity 1.020, otherwise negative.

Phenolsulphonephthalein test 35 per cent. in two hours (intravenously).

| | Per 100 c.c. blood. |
|---|---|
| Total non-protein nitrogen | 49.8 |
| Urea nitrogen | 27 |
| Uric acid | 4 |
| Creatinin | 1.57 |
| Dextrose | 105 |

Red blood-cells 3,500,000, hemoglobin 75 per cent.; leukocytes 7500; neutrophils 82 per cent., small lymphocytes 18 per cent. No red cell changes; no plasmodia.

Wassermann negative.

June 19th: Pericardial rub has disappeared.

June 22d: Much improved. No fever for past two days. Edema of feet and ankles gone. Blood-pressure 105/80.

June 23d: Blood-pressure 118/90.

Phenolsulphonephthalein test 50 per cent. in two hours (intravenously).

June 27, 1925: Patient discharged against my advice. No dyspnea or edema. Lungs clear. Heart smaller on percussion and cardiac sounds are louder. No murmurs. Weight 108 pounds.

*Comment.*—Patient admitted with orthopnea but very slight edema of feet. Complained of no pain but had a temperature of 101° F., a well-marked pericardial rub associated with an enlarged heart. Blood count on admission showed only 7500 leukocytes but with 82 per cent. neutrophils. Blood-pressure was 135/95. The symptoms and signs were suggestive of coronary occlusion, and it is unfortunate that no further blood counts were made. The rub disappeared on the third day and the fever fell gradually to normal in five days. There was also a falling blood-pressure to 105/80, which gradually increased prior to discharge. In spite of the evidence of coronary disease it was thought advisable to administer digitalis in view of the evidence of congestive failure. He received a total of 10½ drams of tincture of digitalis in seven days and made a prompt recovery. The maximum diuresis in twenty-four hours was 56 ounces. The patient, upon discharge, was advised to take a prolonged rest which he did not do.

Second admission: November 14, 1925. Discharged December 2, 1925.

During past two weeks he has been short of breath again and there was swelling of feet and ankles. He has been unable to attend to his work and has to be propped up in bed at night.

*Physical Examination.*—Lies propped up in bed, orthopneic. Face, legs, and feet edematous; cyanosis of lips and finger-nails. Edema of both bases. Heart enlarged as before. At apex, sounds are weak and gallop rhythm present. Second sound split. No rubs. Pulse 120, regular. Blood-pressure 125/90. There is a waxing and waning of the systolic blood-pressure during inspiration and expiration respectively. Abdomen is rather prominent. Liver enlarged. Some suggestion of ascites.

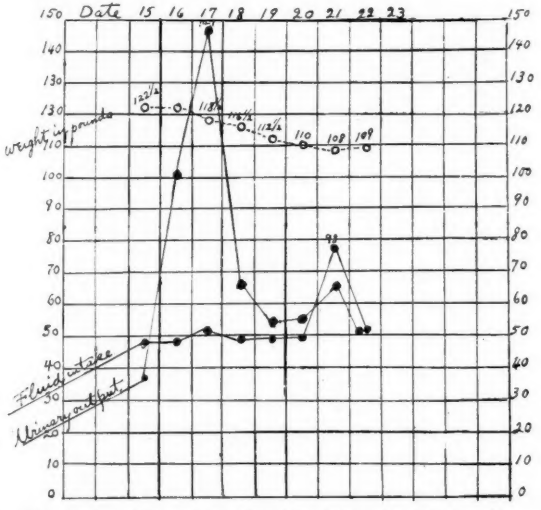


Fig. 216.—Diuresis and loss of weight (edema) following thorough digitalization. Second admission: Myocarditis; coronary occlusion. Intake and output measured in ounces.

December 2, 1925: He was discharged and sent to convalescent home, where he deserted. On the date of discharge his pulse was 76; lungs clear, no edema of extremities, and weight normal.

**Comment.**—Figure 216 demonstrates admirably the diuresis and loss of body weight produced by full digitalization in decompensation with edema. The charts are constructed so that the figures on the left represent the output and intake in ounces and body weight in pounds—the horizontal figures representing days. During this admission he received 10 drams of tincture

of digitalis in six days, then 30 minims daily until discharge. There was obviously no need for further medication.

Third admission, January 15, 1926. Discharged May 1, 1926.

Patient returned to the hospital with congestive heart-failure more marked than on previous admissions. During his long stay in the hospital he showed evidence of decompensation on two occasions due to constantly getting out of bed and walking about against orders. It was impossible to control this patient satis-

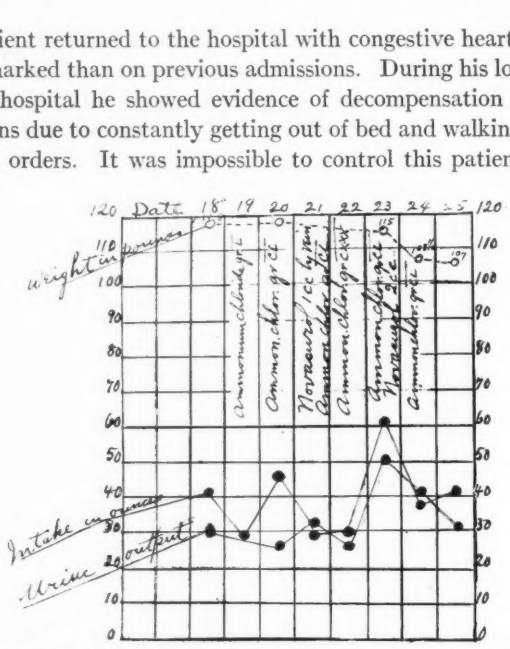


Fig. 217.—Third admission. Patient digitalized. Loss of weight due to toxic gastro-enteritis from novasurol poisoning. Diuresis slight.

factorily because of his low order of intelligence. In these periods of decompensation, digitalis for the first time failed to entirely clear the edema or produce marked diuresis, in spite of the fact that full doses were employed. In view of this fact, resort was had to other diuretics.

Figure 217 shows the result following the use of amnonium chlorid and novasurol. The first dose of 1 c.c. of novasurol by vein administered on the third day of the ammonium chlorid therapy failed to produce any diuresis. He was given a second dose of 2 c.c. of novasurol two days later. This caused some

diuresis, as you will note, but also a violent gastro-enteritis which lasted for three days. His weight fell 8 pounds after the second dose of novasurol, but this loss of weight should, in great part, be attributed to the loss of body fluids by vomiting and purging. Later theobromin sodiosalicylate was administered in conjunction with the digitalis therapy, but without any marked diuretic effect. The diuretin was given, however, in doses of only 30 grains daily. A larger dosage might have been more efficient. The patient gradually improved and insisted on leav-

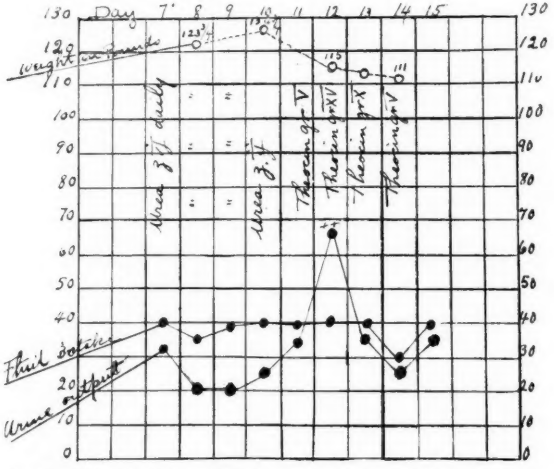


Fig. 218.—Fourth admission. Patient digitalized. Edema of lungs. Liver enlarged. Edema of feet. Alternation of pulse.

ing the hospital. He was advised to do no work and to continue his maintenance dose of digitalis (which he did not do).

Fourth admission November 11, 1926. Discharged January 13, 1927.

On this admission our patient was moderately dyspneic and cyanosed. There was tendency to Cheyne-Stokes respiration. His lungs showed edema of the bases. His pulse was 120; the cardiac sounds were weak, especially the first sound at the apex, and the heart was markedly enlarged. There was further

evidence of myocardial damage by the presence of an alternation of the pulse. The liver was two fingerbreadths below the costal margin. Abdomen distended. Edema of feet and ankles. In this admission full digitalization again failed to abolish the edema. In addition to digitalis therapy, urea was administered from November 9th to 26th inclusive, without any appreciable diuresis or diminution of edema. In extenuation for the failure of urea, it should be noted that the dose was only 24 gms. a day. Considering the patient's comparatively low blood-urea the dose might well have been twice that amount.

On December 11th theocin was given to this patient for the first time. Figure 218 shows that his weight had increased to 126 pounds on December 10th. After four days of theocin in doses varying from 5 to 15 grains per day, there was a loss of almost 16 pounds. On the second day of theocin administration, the chart shows an output of almost 70 ounces in the twenty-four hours. This does not represent the total output as several specimens of urine were lost. The diuretic effect of this drug was truly remarkable. The edema disappeared entirely and his general condition showed marked improvement. Upon discharge he was again strongly advised to continue his digitalis.

Fifth admission February 7, 1927. Discharged March 22, 1927.

Patient's condition on this admission was somewhat better than previous one as he had continued his digitalis (much to our surprise). His chief complaints were shortness of breath and swelling of his feet.

Physical examination revealed moderate dyspnea and cyanosis. Pulse 96, regular. Moderate edema of feet and sacrum. Edema of bases of lungs. On this occasion he was put to bed as usual and the digitalis dosage increased still further until the electrocardiographic curves showed digitalis block and pulse slowed down to between 70 and 80 per minute, without abolishing the edema. Then theocin was given in addition.

Figure 219 demonstrates the efficiency of theocin. A few days' treatment sufficed to clear up the edema, although it will

be noted from the weight chart that the greatest loss occurred during the first two days, as well as the maximum diuretic effect.

Sixth admission April 16, 1927. Died June 3, 1927.

On this admission patient's condition extremely serious. Orthopnea was marked; edema of lower extremities more extensive; cyanosis of lips and finger-nails. Heart markedly enlarged with feeble sounds. Pulse 108. Liver more enlarged. Urine contained traces of albumin, low specific gravity, 1.004. Sediment negative. Blood chemistry (May 4th) was:

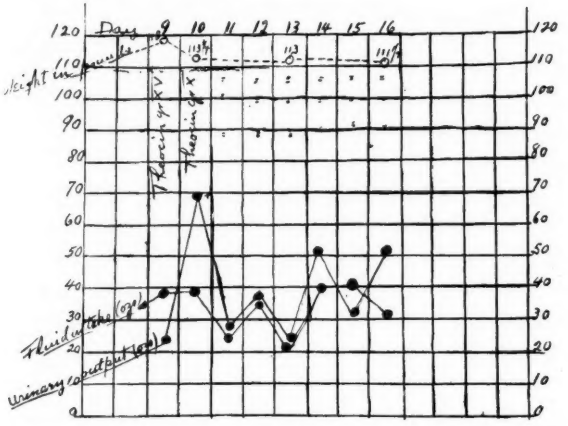


Fig. 219.—Fifth admission. Patient digitalized, but still edematous. Effect of theocin on urine and weight (edema).

| | Per 100 c.c. blood. |
|---|---|
| Total non-protein nitrogen | 31.5 |
| Urea nitrogen | 15.7 |
| Creatinin | 1.3 |
| Uric acid | 5.68 |
| Dextrose | 55 |

Owing to the relatively good condition of the kidneys it was hoped that he might once more be rendered edema free by the use of theocin.

Figure 220 shows the strikingly good response to the theocin in the early part of this admission. Later 1 c.c. of novasurol was

given intravenously without any increase in urinary output. Following this, theocin was again administered with moderately good results, although the end was drawing near. On June 3d he became more cyanosed and extremely dyspneic. He was restless, excited, and delirious. Edema of the lungs became marked. Shortly before death cyanosis developed to an extreme grade on face and extremities. Just before death he vomited a large amount of dark blood.

**Discussion.**—It is not my purpose in the report of the above case to laud the remarkable action of theocin at the expense of other valuable diuretic agents. Novasurol (or merbaphen) has

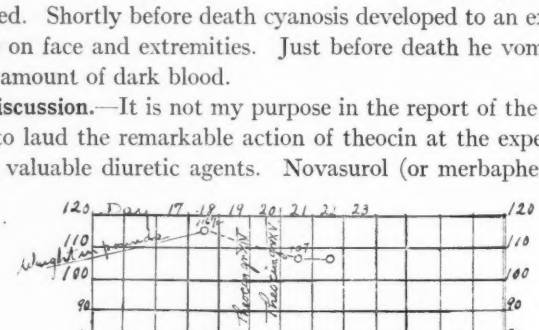


Fig. 220.—Sixth admission. Patient digitalized, but showing evidence of congestive heart failure.

proved its worth in many noteworthy instances. I have chosen this case as an introduction to a few brief remarks as to the status of certain diuretics in the treatment of cardiac edema.

Almost all clinicians agree that the edema associated with circulatory failure is usually best controlled and eliminated by thorough digitalization. There are, however, a small proportion of cases in which, in spite of full digitalization, rest, diet, and other measures, the edema does not entirely disappear. This condition of affairs most frequently presents itself in the cardiac patient who has had repeated attacks of congestive heart-

failure. It is in such instances that the diuretics have an important place. A knowledge of their mode of action, advantages, and short-comings is of the greatest assistance in the handling and management of such difficult cases. In the literature and text-books on cardiology will be found quite a divergence of opinion as to the value of diuretics in cardiac edema. For instance, Eggleston says, "Diuretics are of little value, even in the presence of marked edema, except in such cardiac patients as have relatively little organic renal damage. It is in just such cases, however, that full digitalization is accompanied by the most marked diuresis, so that the need for the xanthene diuretics does not frequently arise." This is a most pessimistic view, and certainly not encouraging to the study of diuretics in cardiac edema. We hope to show that this view is entirely too pessimistic. Christian has studied the effect of diuretics in cardiac edema, especially the xanthin group and is responsible for the following statement: "For the great majority of cardiacs with edema, digitalis is all that is needed. Occasionally it needs to be helped. Theophyllin is the most active of the diuretics for such a patient." In a more recent paper Marvin has shown that "a certain proportion of cardiac patients can be relieved of symptoms by these drugs (diuretics) after adequate treatment with digitalis has failed." He has further demonstrated that these drugs are most effective in the arteriosclerotic hypertensive heart disease group. In this we agree. Time will not permit to enter further into the relative merits of this group of drugs. The diuretics to to be briefly considered are the xanthin or caffein group—urea, ammonium chlorid, and novasurol. The so-called xanthin group consists of caffein, theobromin, and theophyllin. As a diuretic caffein may be disregarded. Theobromin is most commonly employed or theobromin sodio salicylate (diuretin). Theophyllin is best known by the name of its synthetic product, theocin. A derivative of theophyllin that now has quite a vogue is euphyllin. This drug is more commonly employed in its capacity of a coronary dilator. In considering the question of diuresis it is obvious that diuretics will act best in those patients who have relatively little organic renal damage, but it is sur-

prising, at times, to see the response of even badly diseased kidneys. It is also becoming clearer that the diuretic activity of these drugs does not depend entirely upon their action on the kidneys, but that there are also extra renal factors to be considered. The same drug will exhibit in one instance a remarkable diuretic effect and upon another occasion, under apparently the same conditions, will produce no increase in urinary output.

Experience has shown that novasurol is more effective when preceded by and given in conjunction with ammonium chlorid. Ammonium chlorid appears to pave the way for novasurol, possibly by altering the acid-base equilibrium of the body. Keith confirmed Haldane's observation that ammonium chlorid when taken in adequate amount diminishes the normal alkali reserve in the blood and tissues (produces an acidosis). In combination, ammonium chlorid and novasurol cause acidosis, an increase in the chlorid content of the blood, and an increase in the excretion of water, chlorid, and fixed inorganic base, chiefly sodium, potassium, and ammonium. In the diuresis by theocin and digitalis there is an increase in chlorid, sodium, and fixed base similar to that produced by novasurol (Keith *et al.*).

Stieglitz, in a recent illuminating paper, states that the paradox of diuresis by either acidification or alkalinization is open to logical physiologic interpretation. Any deviation from normal physiologic physical or chemical conditions, if the deviation is not so excessive as to be destructive, is a stimulant to activity on the part of the cells to return toward the normal environment. The significant fact is that either procedure, administration of acids or alkalis, causes a deviation from the pre-existing state and, therefore, acts as a renal stimulant. The result of renal stimulation is diuresis. Injured cells, already hyperirritable, are more readily influenced. In nephritis the acid renal cells are made more acid by the administration of alkalis and it is suggested that this added insult is in part responsible for the clinical diuresis so obtained. If the original injury is severe, the additional insult, instead of being stimulating, may be destructive or injurious, with acute exacerbation of the nephritic or toxic edema, as is so often the case. On the other hand, therapy with acid substances

in nephritis tends to acidify the urine more strongly and to diminish the intracellular acidity, bringing the cells closer to their normal state. The effect of the improvement of renal function on the tissues is probably through the control which the kidneys exercise over the acid base balance of the body.

This working hypothesis may be helpful to us in explaining why certain diuretics will act more efficiently following acidification.

The diuretic effect of urea is obtained, according to King, through the stimulus exerted by an elevated urea content of the blood—the rate of urea excretion depending largely on the blood-urea concentration. Urea is not ordinarily a renal irritant, but a contraindication to its use would be an already high blood-urea concentration.

**Mode of Administration of Diuretics.**—Like all good things most of our diuretics have some disagreeable qualities. It is well to weight the advantages and ill-effects of the drug to be selected with great care. For example, theocin is very apt to produce nausea and even vomiting in some patients if its use is prolonged beyond a day or two. It should, therefore, be given over short periods of time and intermittently. On the other hand, euphyllin may be well tolerated for weeks, and can be administered by suppository or by vein. Theobromin and its derivatives may be employed for months with very little disturbance to the digestive tract. The same may be said of urea. Novasurol must be used with caution, as it not infrequently produces renal irritation and violent gastro-intestinal symptoms. Ammonium chlorid in large doses may give rise to symptoms of acidosis. When these drugs are used in proper dosage for a specific purpose, bearing in mind their possible ill-effects, they will be found of great value and at times, life saving.

## CLINIC OF DR. CABOT LULL

BIRMINGHAM, ALABAMA

### HEMOPTYSIS: ITS DIAGNOSTIC IMPORTANCE

THE word "hemoptysis" literally means blood spitting. The mere statement that a person has spat blood calls for details, such as the amount, the color, the frequency of recurrence, and certain other attendant circumstances, before one can even guess intelligently about its source. The color may be pink as in "blood-streaked sputum," bright red or dark red, with or without clots. The amount is very difficult to estimate, and so is the frequency of recurrence, as these data, except in hospital practice, are obtainable only from the patient who is strangely loath to tell the facts.

Ruling out gums and nasopharynx as the possible source, we come at once to the lower respiratory tract, since no especial mention need be made here of the possibility of bleeding from the trachea, the bronchi, the esophagus, or even the stomach as these sources are relatively uncommon and very rarely offer any difficulty. True hemoptysis in old bronchiectasis cases does occasionally occur, but is fairly easily recognized by history and *x*-ray findings, which are characteristic.

The attempt to properly evaluate "blood spitting" is often quite difficult because of the ignorance still prevailing on the part of many laymen and unfortunately even of doctors. There are still a few of us so benighted as to believe a little hemorrhage is good because it carries off impurities, and it is still too common for some family doctors to tell a patient to go on and "forget it." Physicians who deal much with tuberculosis must become very adroit in getting a history of blood spitting. The average patient conceals the fact unless a direct question is asked, and then questions as to the amount of blood and its frequency usually are evaded and a variety of explanations as to its source is offered.

Such persons seem to think the doctor is a prosecuting attorney trying to make them incriminate themselves. Illustrative of this point let me cite a case. A rather robust young ex-service man of more than average intelligence was under treatment for a gastric ulcer, the diagnosis of which was made from a typical history and radiographic study. On coming into the consultation room one day he displayed a handkerchief with blood stains on it. It was not difficult to rule out the gums and teeth as a source of bleeding. Furthermore, the bleeding did not seem related to the ulcer of the stomach as no recognized vomiting or regurgitation had occurred. It was agreed that a nose and throat specialist should examine him. The specialist promptly reported that there was a small erosion in the nasopharynx which could have been the source of the blood. Of a somewhat skeptical temperament I insisted on examining the chest, which—as is so often true in cases of hemoptysis—was quite free from obvious abnormal physical signs. A specimen of sputum was furnished reluctantly by the patient. This, on the next day, showed more blood and, on staining, numerous acid-fast bacilli. Within a few days fine râles could be heard at the right apex, and roentgenologic study confirmed the diagnosis of a right apical tuberculosis, which later became arrested. Some months subsequent to this theyoung man had to be treated surgically because of repeated gastric hemorrhages, and pyloric stenosis. He is now apparently a well man.

The stress laid by such writers as Lawrason Brown on the actual amount of blood in each case of blood-spitting is most important, and the insistence that blood spitting of a dram or more should be regarded as strongly probable evidence of tuberculosis is eminently correct. However, the practitioner who accepts such a dictum and rests his diagnosis upon it alone, failing to exhaust all diagnostic resources to prove his hypothesis, sometimes comes to grief. Repeated moderately large hemoptyses occurring in young subjects with mitral stenosis are sometimes confused with tuberculosis. This mistake while occasionally justifiable in atypical or latent cases, is, of course, inexcusable where the physical findings are perfectly typical of stenosis. A case in point was a strong looking young taxi driver who was

having profuse hemorrhages apparently from the lungs. He reported that he had suffered repeated hemoptyses for years. A most casual examination of the heart showed a thrill, a typical kettle-drum roll with a loud snapping first sound. The lungs, of course, showed nothing suggestive of tuberculosis.

Differentiation of passive congestion of the lungs from other lung conditions may be difficult as illustrated by the following: J. B. W. consulted his doctor because of weariness, breathlessness, cough, and blood spitting. On finding a rapid pulse and an enlarged heart with distant sounds a diagnosis of myocarditis with passive congestion seemed reasonable. Persistence of symptoms with alarming hemorrhage led to hospitalization and *x*-ray. Bloody fluid was aspirated from the chest, revealing a tumor, which on autopsy was found to be sarcoma originating in the hilum of the lung, but extending now into the parenchyma.

In such conditions as lung abscess, bronchiectasis, and neoplasm, hemoptysis is often a serious and puzzling feature, and the underlying cause of bleeding is recognized only when the disease has progressed to the point where it may be diagnosed definitely by history, physical signs, laboratory, and *x*-ray study. The point is that all these measures are often necessary to a correct diagnosis.

The following case presents some difficulties. W. T. C. aged forty-three, had a slight hacking cough, and felt tired for several weeks until one day he had a large hemorrhage from the lungs. The family doctor had an *x*-ray made which showed some "fibrosis," but was in general noncommittal. The sputum was negative. There were slight fever, cough, and repeated hemorrhages. After several weeks in bed the physical signs showed what appeared to be a consolidation at the lobe of the lung with possibility of fluid in the base. The *x*-ray revealed a dense shadow of the right chest. At this stage tuberculosis had been diagnosed by two doctors. Following aspiration of clear fluid, another *x*-ray revealed a blocked bronchus with collapse of one entire lobe. The diagnosis of tumor, probably originating in the bronchus was made, and later bronchoscopy and pathologic examination of section confirmed the diagnosis of a carcinoma of the bronchus.

Before the fatal ending this patient had numerous hemoptyses of varying amounts.

Careful scrutiny of the bloody sputum in acute conditions, such as passive congestion of the lungs from heart disease, pneumonia, pulmonary edema, embolism, and the like, often gives the necessary clue to diagnosis, as every careful clinician can testify.

The conclusion of the whole matter of hemoptysis or blood-spitting may be summed up about as follows. It is a serious thing for a person to expectorate blood and its source always should be sought. It is likely that nine-tenths of all hemoptyses of a dram or more come from diseases of the lungs and by far the most common disease is tuberculosis. Whether the blood results from actual invasion of the lung tissue or the rupture of a tuberculous bronchial gland into a bronchus is of speculative interest largely. It makes no difference that the hemorrhage occurs only once and there follows a long period of perfectly good health. We must insist on the seriousness of the symptom, although we congratulate the victim on the *apparent* healing of the lesion with complete restoration of his health. With what appears to be a greatly increasing frequency of neoplasm of the lungs and bronchi, we should keep this condition in mind in all cases of hemoptysis. By impressing upon our patients the seriousness of this single symptom we shall be able to keep them under observation for longer periods and thereby increase our percentage of correct diagnoses of many of the diseases in question.

CLINIC OF DR. JAMES S. McLESTER

BIRMINGHAM, ALABAMA

## THYROID DEFICIENCY AS A CAUSE OF POOR HEALTH

THE patients of whom I write present a fairly well defined clinical entity. They have three things in common: (1) Among a variety of other disabilities they complain always of easy exhaustion; (2) the basal metabolism is below normal; and (3) on the administration of thyroid substance symptoms disappear and the sense of well-being is improved.

In thus venturing upon a discussion of a group of patients whose disabilities are believed to be due to endocrine deficiency, I hasten to say that I am acutely aware of the necessity for caution. The subject lends itself so readily to the wildest sort of speculation. Endocrinologists have taken a small foundation of known physiologic facts and, drawing for their material largely on the imagination, have built clinical superstructures which are as flimsy as they are fantastic. Before proceeding further, therefore, a frank statement of the limitations of our knowledge in this field would appear pertinent.

The physiology of the several ductless glands as well as their influence upon development and function is fairly well understood, but our ability to influence the work of these glands and to make therapeutic use of their active principles is extremely limited. This can be summarized in a few words: (*a*) Impaired function of the islands of Langerhans with resulting diminution in the output of insulin is the cause of diabetes, and the administration of this hormone relieves the patient in large measure of his handicap; and (*b*) disturbances in the activity of the thyroid gland, resulting in either increased or decreased output of thyroxin, lead to certain characteristic symptoms which can be relieved by appropriate measures, in the latter instance by the administration

of the missing substance. The good to be accomplished by the use of other glandular substances is open to discussion; certainly no satisfactory proof of their therapeutic value has been offered.

The patients of the group to which I invite your attention do not present the well-defined, easily recognized characteristics described in thyroid deficiency of high degree. Sometimes their disability can best be described merely as "poor health." Before the true nature of their trouble is discovered they drift, as a rule, from doctor to doctor and are given various diagnoses. Often they are called neurasthenics. Nevertheless, there are certain disabilities which are common to all, and a few additional troubles which are manifested by the majority, all of which taken together give to the disorder a distinct identity.

The salient characteristic is lack of endurance. These people are unable to stand any sort of strain, physical or mental. While they offer all sorts of complaints, to the observant physician it is evident that easy fatigue troubles them most, and chronic nervous exhaustion is a frequent diagnosis. While this applies to mental as well as physical effort, there is no impairment of the patient's reasoning powers. He merely is not capable of sustained mental effort and is lacking in initiative. He is as a rule fully aware of this disability, and will oftentimes complain that he feels inadequate to meet his daily obligations.

Numbness and vague pains in the legs and arms, particularly after exercise, are frequent. To some patients this is very distressing. Chronic joint pains occasionally occur.

Vague digestive disturbances are often present and may constitute the chief clinical feature. Constipation is frequent. I first became interested in this group of patients when I learned that certain persons with vague gastro-intestinal disturbances, not characteristic of any definite disease, are occasionally benefited in a graphic manner by the administration of thyroid substance.

A few men of this group will complain of loss of libido as the chief symptom, and in other instances inquiry will reveal definite deficiency in this regard. In one of our cases this was the only complaint.

The most impressive feature of the composite picture presented by these patients is a distinct lowering of the sense of well-being. They do not feel well. In many instances a more accurate characterization of the trouble is impossible because all of the symptoms are so vague and indefinite.

The appearance of the patient is not that of typical myxedema True, in a few cases there is noted a facial expression with slight skin changes, such for instance as puffiness beneath the eyes, but I have not seen in the patients of this group the thickened skin, the marked dryness or translucency of the skin, the falling hair, or the characteristic facial expression described in myxedema The person so handicapped is often, though by no means always, overweight. Frequently his muscular development is poor, and he gives the appearance of being flabby. Occasionally we see patients with this deficiency who are actually underweight. It should be added, however, that some of these underweight patients do not properly belong in this group. They are merely the victims of undernutrition, and the lowered metabolism and other evidences of physical disability may be dependent solely upon this.

The patient often looks tired but in conversation he may brighten up and for a time show a normal amount of interest and enthusiasm. This is not for long, however, for sustained mental effort is tiring to him and enthusiasm and interest as a rule are forced.

The circulatory apparatus usually shows certain fairly characteristic symptoms. The pulse is slow and the blood-pressure is usually low. The systolic pressure may be 100 or less. A constant and striking feature is the low pulse pressure. This has been such a constant feature in the patients of this group that when found it suggests always the necessity for a careful reckoning of basal metabolism. Not infrequently we see a systolic pressure as low as 90 with a diastolic pressure of 70 or 75.

I have become impressed with the frequency in these patients of the bottle-shaped heart. This type of heart is in no sense peculiar to thyroid deficiency, but it is interesting that so many of our patients with this handicap have hearts of this shape.

A low-grade secondary anemia is often present, but there is otherwise nothing noteworthy about the blood. The urine often contains albumin. Many of these patients are erroneously believed to have nephritis and are treated for this disease.

The basal metabolism is always low, and furnishes the final criterion by which the patient is judged. A rate which fails to reach the normal by as much as 10 per cent. is ordinarily said to be abnormal, but this margin is probably too small. With the apparatus and technic in clinical use today it seems better to assume arbitrarily that —15 per cent. is the point at which the abnormal begins. All of the patients of our group have had a basal metabolism of 15 per cent. or more below the calculated normal. Often it was —20 to —30 per cent.

Emphasis should be placed upon the necessity for care in estimating the metabolic rate. Complete rest of an hour or longer on a couch in a room alone before beginning the test is advisable. The mental state of the patient during the test is also important; if he is anxious, nervous, and frightened the curve is apt to be irregular and the result untrustworthy. The kymographic tracing in our cases is always scrutinized and unless it shows a fairly straight line indicating even breathing the test is discarded and another taken. We have usually found in such instances that after a few repetitions satisfactory results could be obtained, but occasionally we have encountered a patient who could never learn to take the test placidly and whose basal metabolism we could never accurately determine; these last are reminiscent of the soldiers who cannot wear a gas mask.

**Discussion.**—The disabilities described are probably identical in nature with those of true myxedema, the difference being merely one of degree. However, the vagueness and mildness of the symptoms, and the absence of the graphic skin and other changes seen in true myxedema entitle these patients to a separate grouping. An important difference is in the permanency of the disability. Myxedema represents thyroid deficiency of high degree which is permanent, but the disturbances of which I write are apparently dependent upon a mild degree of thyroid disorder which in many instances is of transient duration.

The cause of this type of thyroid deficiency is a matter of conjecture. It must be admitted that we know no more about this than we do about the causes of pancreatic deficiency; it is possible that like factors are operative in both. The older writers discussed psychic trauma, childbirth, and many other things as possible etiologic factors of thyroid deficiency, but none of these in the light of our present knowledge seems plausible. The one conjecture which seems most reasonable is infection. Just as we believe that repeated infections, unnoticed perhaps, may destroy the islet cells of the pancreas, so is it possible to assume that similar events may cause atrophy of thyroid structures. On the other hand this is little more than theory and it would be more accurate to say simply that through unknown influences,—nervous, chemical, or of other nature—the structural integrity or the functional capacity of the gland may be temporarily or permanently damaged.

It seems futile to discuss from a clinical standpoint the interrelationship of the several glands of internal secretion. Our knowledge is too meagre. The existence of some sort of interdependence of physiologic activity cannot be doubted, but what part suprarenal or ovarian dysfunction, for instance, may play in producing the disabilities of the patients under discussion it is impossible to say. It is tempting, I admit, when lack of endurance is a prominent symptom, to assume that we are dealing with something akin to Addison's disease, or when there is marked menstrual disturbance that ovarian dysfunction colors the picture, but none of this can be proved. We have no means of measurement, and if any such additional dysfunction chances to obtain I doubt if we have dependable means of correcting it. It is best, therefore, to assume in the condition I have described that we are dealing with a fairly well defined disturbance of one organ, the thyroid gland.

The **treatment** of these patients is simple and the results are often graphic. The improvement in the sense of well-being and in mental and physical vigor, as well as the relief of digestive, sexual, or other forms of functional impairment, is often most gratifying. This is accomplished by the use of thyroid substance.

Regarding the appropriate dosage of desiccated thyroid, Plummer administers in true myxedema a large initial dose, 30 to 60 grains (2–4 gm.) which immediately gives a pronounced boost to metabolic activity. Then, after an interval of several days the drug is resumed in smaller doses. In the milder degrees of thyroid deficiency, however, such as are experienced by the patients of this group, it seems advisable to begin with smaller doses and to permit a more gradual effect. True, this takes time but under these circumstances it is probably safer. Usually a period of two or three weeks is required to accomplish the desired results, sometimes longer. Three or 4 grains of desiccated thyroid daily is appropriate in the beginning. Occasionally I have used double this amount for short periods with satisfactory results. At the end of about two weeks, sometimes longer, the effect of the drug makes itself evident; it is advisable then to reduce the dose to $1\frac{1}{2}$ or 2 grains, and again after another two or three weeks to approximately 1 grain daily.

It is not always easy to determine the proper dosage of thyroid substance. The iodin assay of a thyroid preparation is taken as the measure of its potency, but experience has shown that not all standard preparations of thyroid substance on the market are of equal efficacy. It should be added, too, that all people do not absorb the drug with equal promptness and that in those cases where especially large doses appear to be necessary it is probable that the drug is not fully absorbed from the bowel. Changes in dosage will not be immediately felt; therefore, in the effort to properly adjust the dose any contemplated increase or decrease should not be too great, and at least a week or ten days should be allowed to elapse before judgment is taken as to the effect.

The patient's basal metabolism is after all the best guide to dosage. If feasible, frequent estimations of metabolism should be made during this early period of adjustment. Thereafter estimations should be made at longer intervals. Three or four weeks, sometimes longer, is required in the above described procedure to bring the basal metabolic rate to normal. After this has been

reached it is not difficult to establish the amount of the drug which must be given each day in order to maintain this level.

The pulse rate is also a fairly good guide. A pulse rate which is persistently above 90 usually demands a reduction in dosage. Patients often respond to overmedication with headaches, tremor, and other nervous symptoms.

It is probable that there is some regulatory mechanism in the normal person which influences the output of thyroxin and its utilization, and that people who experience impairment of thyroid function are sufferers from a profound disturbance of this mechanism. This may explain why the normal person and the patient with thyroid deficiency do not respond alike to thyroid therapy, for the latter is apt to respond much more readily and in a more graphic manner.

The length of time which thyroid substance must be taken is variable, and in many cases of the group under discussion it is definitely limited. Lowered thyroid activity in these patients is not necessarily permanent. It has been suggested that functional disturbances, either in the gland itself or in the regulatory mechanism which controls its output of thyroxin, are often temporary and that after a time readjustment with complete restoration of function may occur. Clinical experience bears this out. Whether the artificial administration of the active principle promotes such readjustment or whether restoration of function gradually takes place from other causes it is difficult to say, but certain it is that after taking thyroid substance for a few months many of these patients finally reach a point where they no longer need it. It should be added, however, that this is not true of all patients, and that there are a few who seem to need the drug indefinitely.

Thyroxin, the active principle of the thyroid gland, has been used extensively in experimental work, but it is pretty generally agreed that for ordinary clinical purposes it is better to use the desiccated powder made from the whole gland.

It should be emphasized that thyroid substance can do great harm as well as good, and that it should always be administered with caution. If given in amounts sufficient to supply

an existing deficiency, it is beneficial, but if given in excess of this amount, or when there is no deficiency, it is merely toxic. There may be a few exceptions, but it can be stated as a general rule that thyroid substance should not be given unless it is definitely known that the basal metabolism is below normal.

Thyroid substance should be given alone, never in combination with other glandular preparations. There are many polyglandular extracts in use, but fortunately most of them are inert except as regards their thyroid content. Polypharmacy is always bad and it is especially bad when used as a means for steering the ship through "uncharted seas." However, much we may surmise as to the intimacy of physiologic relationship between the several organs of internal secretion, we should endeavor in our therapeutic efforts to confine ourselves to what we actually know. Therefore, it is infinitely better always to give thyroid substance alone.

It should be reiterated that there is danger here of overenthusiasm. Because thyroid substance benefits in a graphic manner a few patients who are deficient in thyroxin there is a temptation to prescribe it with little discrimination. Not every patient who is tired, or is lacking in enthusiasm, or who has a low pulse pressure, or a bottle-shaped heart, or who experiences loss of libido, is a sufferer from thyroid deficiency. The patients who are placed in this category and are given thyroid substance should be selected with care, preferably after metabolic determinations. There are few therapeutic measures which when needed bring more satisfactory results, and there are few which when improperly used are more clearly capable of harm.

## ILLUSTRATIVE CASES

**Case I.**—F. V., a business executive of forty-nine years, has been under my care from time to time for about ten years because of occasional backache and frequent periods of extreme lassitude. Repeated examinations showed no cause for his troubles until it was found two years ago that he had a basal metabolic rate which varied between −17 per cent. and −20 per cent. His pulse rate had always been low, about 60, and the blood-pressure moderately low, 100/60. He was of approximately normal weight and his appearance except for a sallow skin has always been vigorous. Under thyroid medication, 2 grains of the desiccated powder daily at first and then 1

grain daily, his lassitude, backache, and nervous symptoms entirely disappeared. His general sense of well-being and vigor as well as his ability to work has been greatly improved. He is able to stop the drug for long periods, but has found it advisable occasionally to return to it.

**Case II.**—H. B., a female of fifty-five years, gave as chief complaints obstinate constipation a dry, scaly skin, and pains in her limbs. She was somewhat overweight, but beyond this and her dry skin the physical examination showed nothing unusual. The basal metabolic rate was −25 per cent. Thyroid substance in combination with dietary regulation and appropriate exercise promptly put a stop to her constipation and her other complaints.

**Case III.**—C. C., a young man of twenty-eight years, recently married, complained solely of sexual impotence. The salient features in his examination were a rather slow pulse rate, a bottle-shaped heart, and a basal metabolic rate of −30 per cent. He was given desiccated thyroid at first in rather large doses and later in smaller doses, and soon reported that his chief complaint had entirely disappeared. (There is also included in this group the case of still another man with identical complaint and a basal metabolic rate of −28 per cent. who experienced gratifying improvement on taking thyroid substance.)

**Case IV.**—W. C., a female executive of fifty years, gave the general impression of being a typical neurasthenic. She was extremely apprehensive and on the appearance of the least disturbance, real or imaginary, she always hurried to the physician for relief and explanation. Everything was worse when she was fatigued, which was of frequent occurrence. She occupied a responsible position and was efficient in her work, but always gave out easily. Examination revealed nothing unusual except some elevation of blood-pressure, 160/90, which she stated had previously been even higher; it was thought perhaps that this was related to the menopause through which she was passing. Her basal metabolic rate on each of several tests was persistently low, usually −18 per cent. or −20 per cent. Since beginning to take thyroid substance she has recovered for more than a year a large part of her equilibrium, is able to continue her work with less fatigue, and does not complain of her former aches and pains.

**Case V.**—J. E. S., a married woman of forty-five years, complained of all sorts of vague digestive disturbances. She drifted from one physician to another, and was properly regarded as a neurasthenic. She was exhausted by the least effort and sighed as she talked. She was somewhat overweight and had a slow pulse with low blood pressure and pulse pressure. Her basal metabolic rate was − 20 per cent. Thyroid substance gave her a wonderful boost, corrected her digestive disturbances, and put a stop to her complaints.

**Case VI.**—L. A. E., a female school teacher of forty-eight years, complained of pains almost everywhere, chiefly in the abdomen. Ureteral stricture had been diagnosed and she had acquired the catheterization habit so

often seen in neurasthenic women. She was slightly overweight and was experiencing the menopause. Her mental state was distinctly suggestive of the manic-depressive type. When it was found that her basal metabolism was −24 per cent. and she was given liberal doses of thyroid substance. In addition it was insisted that she no longer have the ureters dilated, and a certain amount of psychotherapy was attempted, whereupon she became much better and the pains disappeared. Whether the thyroid deficiency played a part in her psychosis it is difficult to say, but the latter was entirely relieved soon after when this deficiency was corrected.

**Case VII.**—I. W. C., a female of thirty-nine years, complained of great weakness and of digestive discomfort whenever she ate anything. She had been starving herself for several years, and was markedly undernourished. The physical examination showed nothing unusual beyond secondary anemia and a state of inanition. The basal metabolic rate was −22 per cent. It was recognized that this lowered rate was possibly due in part if not wholly to starvation. Nevertheless, she was given ½ grain of thyroid substance three times daily together with an abundant, well-balanced diet, whereupon she not only gained weight but lost all of her digestive disturbances. In support of the view that actual thyroid deficiency rather than starvation was primarily responsible for her troubles it should be added that previous to this time she had *experienced a "rest cure" with overfeeding, but little* or no improvement.

**Case VIII.**—F. B., a young woman of twenty-eight years, a social service worker, complained of general malaise, numbness in the arms, and puffiness beneath the eyes. She has always been ambitious, of pleasing personality, and very efficient. She has found it necessary, however, to take frequent vacations, always because she was thoroughly exhausted and "too tired to work." Unfortunately, at the end of each vacation she has usually been just as tired as previously. Her skin was of a somewhat sallow appearance, and there was a slight tendency toward edema beneath the eyes, but she has not shown the thickness or translucency of the skin or the falling hair described in myxedema. She puts on weight readily but through dietary restriction has managed to keep her weight fairly well within normal limits. On examining her first three years ago it was found that her pulse rate remained approximately 60 to the minute, and that the blood-pressure and pulse-pressure were persistently low, systolic 85, diastolic 60. The basal metabolism on each of several tests was uniformly low, about −35 per cent.

After several months of persistent thyroid therapy this patient showed marked amelioration of symptoms. She was given for a short period 9 grains of desiccated thyroid daily; subsequently this was reduced to 4 grains and finally to 2 grains daily, which last dose she took for eighteen months. The pulse rate when she is under the influence of thyroid substance is about 80 to the minute with a normal blood-pressure, approximately 120/80. A year's treatment was required to bring the metabolic rate to the calculated normal. When this rate obtains she feels well, has energy and initiative, and can do her work efficiently and with ease. If thyroid medication, how-

ever, is stopped for longer than two or three months she again experiences her old symptoms.

It is possible that this patient could more properly be said to have myxedema, although her mental alertness and many other characteristics were against this. Also it is recognized now that our method of thyroid therapy with her was in the beginning too dilatory; had we at the outset given her the large doses advised by Plummer we would no doubt have achieved quicker results.

## CLINIC OF DR. HUGH J. MORGAN

NASHVILLE, TENN.

# INDUCED SYPHILITIC MENINGITIS (MENINGO-RECURRENCES)*

THE patient who is the subject of this discussion is suffering from a very prevalent disease. Any disease which numbers its victims by the thousands commands consideration. When we recall that syphilis numbers its victims by the millions it becomes apparent that medical men must have more than a passing interest in it. I shall not discuss at length the prevalence of syphilitic infection. It is found in every walk of life, in white and in black, in rich and in poor, from infancy to old age. The Treponema pallidum recognizes no social or racial barrier. The epidemic of syphilis which swept over Europe in the fifteenth century scattered treponemata so widely that now no race or country is free from the disease. The United States with its 7,000,000 to 9,000,000 syphilitics is certainly no exception to this statement.

It is obvious that we must regard syphilis as a generalized infection—not as a venereal disease. I am sure that you will agree that the venereal aspect of the disease is unimportant as far as damage to the individual's body is concerned. Syphilis is not a genito-urinary disease, except in so far as its initial lesion is usually a trivial self-limited sore on the genitalia which appears days after generalized infection has occurred. Nor is acute syphilis a dermatologic disease except in so far as it usually leads to the development of a fleeting and ofttimes inconspicous rash. Syphilis is a generalized infection—a disease of the body as a whole—and of the *whole* body—the most important lesions of which are those developing in and around the heart and blood-vessels and

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in the central nervous system. It should be constantly remembered, however, that this disease limits itself to no single system or structure.

Before proceeding to the consideration of the case I wish to remind you that immunity is a factor in syphilitic disease as in other infections. In the untreated disease the patient's resistance is of prime importance.[1] Without the development of this resistance, which spontaneously terminates the secondary stage of the disease, the individual would probably succumb to an overwhelming, generalized treponemal infection just as the syphilitic fetus succumbs. Thanks to this natural force the body, unaided, usually checks the infection and passes into a period of latency or quiescence. This, it must be remembered, is an immunologic reaction capable of being modified by any factor interfering with the natural development of the disease, as antisyphilitic treatment.

The case to be reported presented, when first seen, important diagnostic problems, but is of especial interest because it illustrates impressively the dangers incident to the haphazard, casual, inadequate treatment of early syphilis. That such treatment may operate to the detriment of the patient is illustrated in this case—the way in which it operates will be suggested in the discussion which follows the case report.

**Case Report.**—The patient is a traveling salesman twenty-five years of age and unmarried. He was brought to the hospital in an ambulance. He was unable to give a connected account of his troubles, and only an incomplete history was obtained from his mother.

Nine days before admission to the hospital he felt fairly well with the exception of slight headache. The latter had been present for some days but had not interfered with his work. On the evening of the ninth day before his admission he retired to his hotel room and went to bed. He complained to a friend on saying good-night that his head had ached badly all day and he retired early for this reason. The next morning he was found on the floor of his room in a dazed state, disoriented as to time and place, and with no recollection of what had transpired during the night. There was an abrasion on the tongue and lip and a superficial scalp wound was present. These findings led the attending physician to the conclusion that he had had a generalized convulsive seizure and he was placed in a hospital. Here he remained for two days. During this time he was restless, irritable, and altogether incorrigible. He complained bitterly of persistent headache. On the

third day he left the hospital unimproved and drove his car to Nashville, a distance of 125 miles. On arrival here he was beside himself with headache. The usual remedies were of no avail. For six days he was unmanageable and his mental state was such that his mother questioned his sanity. On the day before his admission to the hospital his head ached so intensely that finally in desperation, he procured whisky and drank himself into a state of unconsciousness. The following morning he was aroused with difficulty. He continued to complain bitterly of headache and talked irrationally at times. He remembered nothing that had transpired the previous day. Just prior to his admission to the hospital he was conversing with his mother when suddenly he became quite pale. Immediately his hands and arms became rigid, his head was drawn to the right side, and conjugate deviation of the eyes to the right occurred. No clonic movements were observed and there was no loss of sphincter control. In the course of a few moments his body relaxed and he began talking in a disconnected, incoherent fashion. He came under observation June 24, 1926, nine days after the onset of his illness and on the day of this, his second, convulsive seizure.

On admission to the hospital and after the headache had been relieved to some extent by large doses of codein, caffein, and phenacetin, the following past history was obtained: In January, 1926, following exposure, he consulted a physician in a neighboring city because of the development of a painless, circumscribed, ulcerated lesion on the penis. Material from the ulcer was examined only once by the dark-field method and no treponemata were found. A blood Wassermann examination was made and reported negative. He was assured that the lesion was not syphilitic in nature, and following chemical cauterization it rapidly resolved.

In March (six or eight weeks later) he consulted a local physician. An examination by him revealed characteristic skin manifestations of early syphilis. A diagnosis of syphilis was then made and energetic antisyphilitic treatment was instituted. After he had received three injections of neo-arsphenamin he made a business trip to a nearby city and consulted there a physician of his acquaintance for the purpose of continuing antisyphilitic treatment. Examination at that time revealed perfectly normal skin, showing no rash whatsoever, and a Wassermann examination of his blood-serum was made and reported negative. He was informed by this physician that his case had been incorrectly diagnosed and that antisyphilitic treatment should be discontinued. This advice was gratefully accepted. The last of the three neo-arsphenamin treatments was given in the latter part of March or in the first part of April. The patient was not clear as to exact date.

For a period of a little over two months (perhaps ten weeks) after cessation of treatment the patient remained symptomless. Then occurred the headache previously referred to, and shortly thereafter, the convulsive seizure which initiated the illness leading to his admission to this hospital.

His temperature was 98° F. on admission but rose shortly to 100° F., and varied between these figures during his stay. The pulse rate varied between 80 and 90 per minute. His respirations were normal. He was restless, apprehensive, easily excited, and tremulous. He complained that his "mind seemed clouded" and that he could not remember clearly recent events. He

suffered intensely from generalized headache which could only be temporarily and partially relieved. The skin and mucous membranes were normal except for the partially healed abrasions of the tongue, cheek, and scalp. A few shotty glands were palpable in the inguinal and posterior cervical regions. No generalized glandular enlargement was present. The remainder of the general physical examination revealed the following positive findings: The peripheral vessels were everywhere abnormally thickened and the aortic second sound had a distinctly ringing, metallic quality; the blood-pressure was 120/60; a soft, pigmented scar was present in the sulcus near the frenulum. The only positive findings on neurologic examination were distinct hyperemia of the retinæ with fulness of the veins and indistinctness of the borders of the optic disks, though physiologic cupping was present. There were no signs of meningeal irritation except brisk, though not distinctiy hyperactive reflexes. The usual examinations of the urine and blood revealed normal findings. The Wassermann reaction with the blood was negative with both alcoholic and cholesterinized antigens. The Kahn test for syphilis was doubtful, distinct precipitation occurring in only one of the three dilutions of antigen used. A lumbar puncture was performed on the day of admission. The cerebrospinal fluid was under definitely increased pressure and contained 80 cells per cubic millimeter. The test for globulin was strongly positive and the colloidal mastic test was positive, showing reaction No. 4 in one tube. The Wassermann reaction was positive with 1 and 0.5 c.c. of fluid.

The case may be summarized as follows: A man twenty-five years old, admitting exposure, developed a painless lesion on the penis which was considered non-syphilitic. Approximately two months later a diagnosis of secondary skin syphilis was made, treatment instituted and continued until three injections of neo-arsphenamin had been received. At that time on the advice of another physician and because of the absence of clinical or serologic (blood) evidence of syphilis, treatment was discontinued without immediate harmful effect. Eight to ten weeks later headache, convulsive seizures, disorientation and mental confusion developed. Ophthalmoscopic examination revealed indistinct optic disks and congested retinæ; the reflexes were brisk. A low fever was present. The cerebrospinal fluid examination gave conclusive evidence of syphilitic meningitis.

A diagnosis of syphilitic relapse or recurrence was made. The case clearly belonged to the "meningeal recurrence" or "meningorecidive" group. Antisyphilitic treatment resulted in a prompt symptomatic cure of the meningitis with return of the spinal fluid findings to normal after approximately 8 gm- of neo-arsphenamin and 7 grains of the salicylate of mercury. Intensive treatment was continued.

**Discussion.**—In considering the diagnosis of this case one is impressed with the following fact: The signs and symptoms of clinical neurosyphilis developed within five months of the appearance of the chancre, and within eight or ten weeks of the last neo-arsphenamin treatment. As a rule, clinical evidence of

neurosyphilis in untreated individuals occurs late in the disease, separated from the primary and secondary stages by an interval of at least a year, and usually by an interval of several years.

The case furnishes a classical example of recurrent or relapsing early syphilis. It may prove of interest to consider briefly this post-therapeutic accident: Recurrent early syphilis. The word "recurrent" implies that the natural development of the disease in the body had been checked temporarily. Therefore, the development of aortitis, tabes, gummata or any other late manifestation of syphilis in a previously treated individual represents recurrence or relapse. It is not this type of recurrence that we are concerned with in the case at hand. The recurrence here was an early recurrence, a syphilitic lesion which had not been checked or delayed for a long period of time by treatment, but one which we believe was actually precipitated by inadequate treatment.

Osler has said that "no disease, syphilis least of all, follows any rules in its clinical phenomena." However, if the natural development of syphilis in the human is not interfered with by treatment the sequence of events is fairly orderly, and can be predicted with considerable certainty. Let us briefly review this development. Shortly after inoculation with the virus and several days before the appearance of the chancre a general dissemination of treponemata occurs throughout the body. The chancre, or initial lesion, then appears at the site of inoculation, persists for three to six weeks, and finally resolves. At this time, or even before the disappearance of the chancre, skin lesions may become obvious—manifestations of the previous general dissemination of the virus. Thus the secondary stage is reached with its skin, mucous membrane, bone, lymph-gland, and central nervous system signs and symptoms. It is at this time in the disease that the actual number of treponemata in the body is probably greatest. However, in the course of a few weeks the defensive mechanism of the host begins to assert itself. Due to immunologic processes little understood the destruction of organisms begins and continues until only isolated, more or less walled-off remnants of the infection remain. The widespread

lesions of the skin and mucous membranes disappear, the adenopathy recedes, headache, restlessness, and other symptoms of central nervous system involvement are no longer present. The individual, in the vast majority of cases becomes able to cope well with the remaining localized collections of organisms, and so passes into what is called the latent stage. The infection lies dormant and the patient is symptomless. As times goes on these localized lesions may experience a recrudescence and become of clinical importance (as in the aorta) or they may act as feeders of treponemata to other body tissues in regions remote from them. These tissues, now specifically sensitized, react with a rapidly proliferative granulomatous response—the gumma. Thus the tertiary stage of the disease becomes manifest.

The above brief survey of the progress of the disease in an untreated case of syphilis is given in order to again emphasize the fact that a defensive mechanism operates in syphilis—that there develops a real though usually incomplete immunity to the disease. This defense mechanism rarely, if ever, completely eradicates the agents of the disease; when once they are entrenched I know of no reported case of spontaneous cure of syphilis. How ever, it reduces the infection from an acute, generalized, fulminant one to a chronic, localized, quiescent one. As I have previously said, without this mechanism the untreated syphilitic would probably succumb to the generalized treponemal infection, just as the syphilitic fetus or infant succumbs, its body tissues literally alive with parasites. With this mechanism the untreated syphilitic spontaneously gets the infection in hand, destroys an innumerable number of treponemata and localizes the remainder in a fashion that is compatible with months and years of life.

Moore and Keidel[2] have recently pointed out that poorly-planned or inadequate treatment robs the patient with early syphilis of this immunity. If the natural course of the infection is interrupted by the administration of small, infrequent, subcurative doses of treponemicidal drugs this natural provision for destroying and localizing the infection is thwarted, and this in an individual who still harbors parasites. It seems inevitable

that patients so treated should relapse—and so they do. In a series of 196 cases of early syphilis recently reported by Moore and Kemp,[4] 175, or 89.2 per cent., relapsed. Only 11 per cent. were cured. None of these patients had received more than 9 doses of arsphenamin and little or no mercury. Of the 175 cases exhibiting recurrences, 78, or 44 per cent., were cases of recurrent early syphilis, and approximately one-half of these were examples of acute involvement of the central nervous system (meningo- and neuro-recurrences). We may predict then that an appreciable number of early syphilitics who receive antisyphilitic treatment, but in obviously inadequate doses (less than 9 doses of arsphenamin), will develop acute syphilitic cranial nerve or meningeal disease. The practical importance of the recognition of this fact by those engaged in the treatment of early syphilis and by the patients themselves, is illustrated by the case under consideration. It is obvious that this man would have been infinitely better off if he had received no treatment at all. His inadequate treatment served only to forestall the development of his natural defense mechanism. Deprived of the latter, relapse of a more serious nature occurred.

It hardly seems logical for this discussion to be closed without reference to some definite method of treatment of early syphilis. In the syphilis clinic at the Vanderbilt University Hospital Dr. P. G. Morrissey has adopted the plan of therapy employed by Keidel and Moore. This is a method of "continuous" treatment, consisting of courses of arsphenamin separated by overlapping courses of mercury. The underlying principle of this plan is the continuous administration of a treponemicidal drug during the early stage of the disease. This is persisted in for at least one year after the disappearance of all lesions and after the reversal of blood and spinal fluid Wassermann reactions. The patient is then placed on probation with frequent physical and serologic examinations. But it is not my purpose to advocate any particular drug or method of treatment. Journals and textbooks abound with methods.[3] Suffice it to say that we have in the arsphenamins, mercury, and bismuth, drugs of proved value—drugs which are actually curative when used early in the dis-

ease. Methods for their proper administration are available. The greatest need in the care of early syphilis is the adoption of some method—I am tempted to say any method—and its use with enthusiasm and determination. Without this the patient will miss the chance for cure. But that isn't all! It is necessary to remember that inadequate, haphazard treatment not only may deprive the individual with early syphilis of possible cure, but it may thwart the natural protective mechanism and thereby favor a relapse—an exacerbation of the disease such as has been described in the case cited.

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3. Stokes, J. H.: Modern Clinical Syphilology, W. B. Saunders Company, 1927.
4. Moore, J. E., and Kemp, J. E.: The Treatment of Early Syphilis, Johns Hopkins Hosp. Bull., xxxix, 16, 1926.

## CLINIC OF DR. JOHN H. MUSSER

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# THE LEUKOCYTIC RESPONSE TO THROAT INFECTIONS

THE most bizarre and peculiar leukocytic blood-pictures are often seen in association with throat infections. Within the past comparatively few years several new clinical entities have made their appearance in the field of medicine as a result of more accurate studies of the blood, during the course of throat infections, than have been made in the past. These clinical syndromes vary considerably in their several manifestations and are for the most part not likely to be confused when they stand out in the most characteristic form. On the other hand, cases in which the picture is not as sharply defined as the usual classical presentation, sometimes cause considerable diagnostic difficulty. Sometimes, even the picture itself is not recognized by its original painter. Schulz[1] who first described agranulocytic angina, in 1922, in discussing some of the cases of the disease that had been lately reported in German literature, questions most seriously the diagnosis made by the several different physicians, recognizing only a few of them as true agranulocytic angina. It would seem, however, that he is entirely too critical in his argumentation. Degrees and grades of disease are so common and clear cut, absolutely typical pictures are so rare, that it seems he should recognize some alterations in the picture he originally described. It does not follow that because the patients he enumerated went on to death that all patients should die with the disease, a criterion upon which he lays considerable stress. Weiss[2] contends, to me

[1] Schulz, W., On Different Throat Infections, Deutsch. med Wchnshr., 1922, 48, 1495.

[2] Weiss, J., Mutual Relations between Agranulocytosis Acute Leukemia and Septic Infection, Wien. Arch. f. inn. Med., 1927, 14, 303.

correctly, that only two criteria characterize the disease as an entity: a clinical criterion—necrotic inflammation of the tonsils, gums, and mucous membrane of the mouth—and a hematologic criterion—serious diminution or complete absence of the granulocytic cells.

## LEUKOCYTIC PICTURE

Infection of the throat may give four changes from normal in the leukocytic picture:

1. Polymorphonuclear increase.
2. Mononuclear increase.
3. Leukopenia and diminution in, or absence of, granulocytes.
4. Leukocytosis and relative hypogranulocytosis.

Employing a broad definition for the word septic, all these four reactions may be the result of septic infection of the throat and mouth. That much is known, but the type of the infection is not known nor can the response to certain infections about which we do know something be predicated by the observed local manifestations.

**Polymorphonuclear Increase.**—In the first type of response, which may be exemplified grossly with an out-and-out pathogenic infection such as quinsy, there is a hyperleukocytosis and a hypergranulocytosis. Diphtheria also gives somewhat the same reaction, but not to the same extent. In a series of cases that were recently studied by Sowell[1] for the purpose of determining the effect of antitoxin on the leukocyte count, it was found that the total number of leukocytes in 33 cases was over 12,000 in 27 cases and under 11,000 in 6 cases. In the greater number of cases the count was over 20,000 with a pronounced increase in the number of polymorphonuclear cells. Of the 6 cases that were low, 2 of them presented a low polymorphonuclear count, both total and absolute. It is quite possible that these cases had a mixed infection and a type of response which might come under classification 3. That is to say, the ubiquitous diphtheroid, present in the mouths of so many individuals, ob-

[1] Sowell, R. F.: The Effects of Antitoxin on the Leukocytosis in Diphtheria, Med. Clin. N. Amer., 1928, 11, 1293.

scured the diagnosis, which was called diphtheria on the basis of positive cultures, when in reality we were dealing with one of the other types of mouth infection associated with leukopenia and hypogranulocytosis. This seems highly probable in his case No. 23, with a total count of 9500 leukocytes per cubic millimeter and a differential count of polymorphonuclears 41 per cent., lymphocytes 41 per cent., and monocytes 18 per cent.; in case No. 13, with a total count of 10,750, there was a differential count which showed polynuclears 37 per cent., lymphocytes 43 per cent., and monocytes 19 per cent.; while in case No. 10 the total count was 3500, but 75 per cent. of these cells were polymorphonuclears, thus showing an absolute decrease, but a relative increase of polymorphonuclears. In these cases the hematologic findings were at such a variance from the ones in patients with diphtheria, they might well have been misdiagnosed. In this connection I would call attention to the frequency with which the large mononuclear, the real monocyte of the blood, is increased in diphtheria; counts of 12, 13, 15, 18, per cent. and higher are not unusual, so that there is both an absolute and relative increase in the number of these cells in many cases of this disease.

In streptococcic sore throat and in the biologically closely related infection, scarlet fever, a hyperleukocytosis with polymorphonuclear increase is the customary finding. Examples of this type of infection and the white cell changes will be given in the case reports.

**Mononuclear Increase.**—The second reaction to throat infection is exemplified by the disorder, infectious mononucleosis. In this condition we have the occurrence of sore throat, enlarged lymph-glands, and a most interesting white blood-count, in which there is a reduction in the number of granular cells, slight it is true, but absolute, and with a relative and absolute increase in mononuclear cells. These mononuclear cells are of three types, according to Longcope[1] the usual small lymphocyte, the large mononuclear identical with the large monocyte or

[1] Longcope, W. T.: Infectious Mononucleosis (Glandular Fever) with a Report of Ten Cases, Amer. Jour. Med. Sci., 1922, 164, 781.

transitional cells of normal blood, and a mononuclear not usually met with in normal blood. These cells are monocytes and even with the oxidase reaction do not show the presence of granules. This condition is caused by an unknown etiologic agent and it is differentiated largely from the preceding two conditions by the absence of ulcerative lesions in the mouth. The organism of Vincent and the spiral organisms may or may not be present, but in none of the cases does the appearance of the throat resemble a Vincent's angina. Furthermore, this is not a leukocytic response peculiar to the individual, but a specific one, as Sprunt and Evans[1] reported in their series a patient in whom subsequent infection resulted in the usual polymorphonuclear response.

**Leukopenia and Hypogranulocytosis.**—The third reaction occurs most beautifully in an interesting disease known as agranulocytic angina. In this condition, according to Schulz (*loc. cit.*) we have a syndrome of absence of granulocytic cells in the peripheral blood, jaundice, and a severe stomatitis, occurring for the most part in middle-aged females in whom there was absence of hemorrhagic diathesis, septic foci, and leukemia. These cases terminate fatally. In a few of the cases pyogenic organisms have been isolated and almost invariably have been found Vincent's organisms and spirochetes. In this same category belongs a disease to which on the whole comparatively little attention is paid from the point of view of hematology, that is, Vincent's angina. It is hard to get any definite information as to an accurate series of blood-counts made on patients with Vincent's angina. Simon, for example, says that the leukocyte count averages around 10,000. Weiss says that usually there is a decline in the polymorphonuclears and simultaneously an increase in monocytes and lymphocytes when the deposit is of a membranous, necrotic character in which the examination of the contents shows the presence of typical spirilla and fusiform bacteria. In this condition there is often a reduction in the total number of leukocytes, though this does not necessarily follow.

[1] Sprunt, T. P., and Evans, F. A.: Mononuclear Leukocytosis in Reaction to Acute Infections, Johns Hopkins Hosp. Bull., 1920, 31, 410.

This same type of reaction, leukopenia with hypogranulocytosis, is seen in other conditions in which the bone-marrow is inadequate to respond to normal stimuli. Thus in aplastic anemia, an anemia which is secondary to a primary bone-marrow dysfunction of unknown cause, one of the primary diagnostic features is the reduction in total leukocytes, and a marked absolute and relative diminution in the granulocytes. The same picture is observed in benzol poisoning and has been more carefully studied in Roentgen-ray workers and in experimental animals. The primary effect of these radio-active rays is a stimulative one; the late effect, destructive, with a reduction of the circulating leukocytes with a relative lymphocytosis. These conditions, however, are hardly germain to the present discussion, as septic mouth conditions may be present only as a non-related lesion.

In sepsis, according to Kastlin,[1] Türk, Marchaud, and Stursberg have described cases with gangrenous stomatitis, neutrophilic leukopenia, relative lymphocytosis, thrombopenia, and hemorrhagic diathesis. Shulz does not consider these cases of agranulocytic angina. Weiss does, as do most writers. Perchance they were the response observed at times in severe sepsis. They were not cases of infectious mononucleosis; the severe angina going on to death would rule out this disorder.

### LEUKEMIC REACTION

In the fourth category is placed acute leukemia, a condition which very generally is associated with ulcerative mouth lesions, with *Bacillus fusiformis* and spirochetes in association, and with a simultaneous relative or absolute hypogranulocytosis. In this condition the usual concept is that there is an increase in all the number of cells. On the contrary such is not the case; there may be a diminution actually in the number of granulocytes in the peripheral blood. It is perhaps unfair to consider acute leukemia in the list of septic infections, but this is done more with the idea of discussing septic conditions of the mouth rather than

[1] Kastlin, G. J.: Agranulocytic Angina, Amer. Jour. Med. Sci., 1927, 73, 799.

the etiologic significance of some factor of which we are ignorant. As a matter of fact it is the general tendency to believe that leukemia is a constitutional reaction in a familial strain, peculiarly susceptible to the disorder. Moreover, it may be that in individuals such as this, the response truly is a septic one rather than one of which we know nothing. One of the present day and possibly wrong conceptions of leukemia is that it is a septic infection with a leukemoid blood reaction and that the two conditions of acute leukemia and chronic leukemia are not related and that acute leukemia in its course and its manifestations, clinically, is a totally different disease from the ordinary chronic lymphatic leukemia. The only reason that it should be called leukemia at all is the fact that there is a leukemic reaction; that is to say, a blood-picture which shows a large number of so-called lymphocytes, or more strictly speaking, of lymphoblasts.

Another interesting feature of acute leukemia is that the marked increase of white cells does not occur until the sore mouth is present. Weiss (*loc. cit.*) writes that hypogranulocytosis or agranulocytosis cannot be the cause of the necrotic inflammation of the mucous membrane, but that both of these symptoms, the necrosis of the mucous membrane and the blood-picture, are caused by the septic infection.

Leukemoid blood-pictures, according to Krumbhaar[1] are relatively common, but in such diseases as measles or whooping-cough, in which he gives blood-counts, there is not an absolute diminution of the granulocytes. In atypical lymphocytosis with infection, such as Cabot has recorded as well as Krumbhaar, there was a hypogranulocytosis, but these cases may have been infectious mononucleosis. Furthermore, in none of these cases was there the sore mouth, the feature with which we are primarily interested in conjunction with abnormal hematology.

### VINCENT'S INFECTION

In many of these throat infections the presence of Vincent's organisms in enormous numbers is an outstanding feature. It is

[1] Krumbhaar, E. B.: Leukemoid Blood-pictures, Amer. Jour. Med. Sci., 1926, 172, 519.

one of the rather interesting observations in medicine that when this bacillus, with its brotherly spirochete, is present in mouth lesions it seems to have a definite tendency to be associated with a peculiar and unusual reaction of the granulocytes. There has never been any proof, however, that this is in any sense specific. However, it happens with such a great degree of frequency that it would appear to be more than a coincidence. Certainly in these ulcerative lesions of the mouth and throat, there is often a hypogranulocytosis and often an absolute increase of mononuclears, with usually a relative increase in these leukocytes.

The usual idea and conception is that the organisms are secondary invaders or normal inhabitants of the mouth and that they bear little relationship to many of the diseases in which they are found. In such a common ordinary and every-day disorder as pyorrhea alveolaris, *B. fusiformis* and spirochetes were found in all the smears from 201 cases.[1] Existing as these organisms do in so many dirty mouths, it is not to be wondered at that when ulcerative lesions occur, lesions which favor their growth, they should be found in such plentiful numbers.

But in mouth and throat infections without ulceration and necrosis, Vincent's angina, if real Vincent's angina exists without ulceration, the condition is purely a local one without systemic or hematopoietic response or with practically none, whereas when ulceration occurs there is invariably constitutional disturbance.

As illustration of the unique response to throat infections of the peripheral blood-count, some case histories will be given in abstract.

## CASE REPORTS

### I. Leukocytic Reaction to Throat Infection: An Increase in the Total Number of White Cells with a Marked Preponderance of Granulocytes (Polymorphonuclear Leukocytosis).

**Case I.**—R. H., a small boy aged three years was admitted to the hospital on account of scarlet fever of several days' duration. The temperature was 104° F. on admission, with correspondingly rapid pulse. The whole posterior pharyngeal wall was very much inflamed and hyperemic, with enlargement of the cervical lymph-glands. Examination of the blood showed a total red count of 4,375,000, with a low hemoglobin. The white cells

[1] Fisher, J. F.: Pyorrhea Alveolaris: The Rôle of Certain Microörganisms Found in the Lesions, Amer. Jour. Path., 1927, 3, 169.

numbered 12,500 per cu. mm. Polymorphonuclears were 89 per cent. The throat cultures were all negative for diphtheria.

**Case II.**—A month before the admission of this boy to the ward, his brother, A. H., was admitted with what was supposed to be streptococcic sore throat of some days' duration. This little colored boy was four years old. Eleven days before he was admitted he became sick with high fever and a rash. Two days later a membrane appeared on the tonsils. Despite diphtheria antitoxin his temperature continued and the throat failed to clear up. When he was admitted to the contagious disease service he was found to have a dirty-appearing, widespread ulceration of the pharynx. His total count upon admission was 19,400 white cells, which gradually fell in the course of ten days to 12,000 and the polymorphonuclears, which were 80 per cent. fell to 68 per cent. Improvement of the condition continued and the patient was discharged apparently in perfect condition.

These two children evidently had scarlet fever and showed the leukocytic response that goes with this condition of streptococcic infection of the throat, whether due to a specific or a non-specific type of organism. Innumerable other cases of leukocytosis with polymorphonuclear increase could be recounted. Such a blood-picture is so common in peritonsillar or retropharyngeal abscess and diphtheria that it hardly seems worth while to go into such case histories.

## II. The Response to Throat Infection Characterized by the Formation of an Excessive Number of Mononuclear Cells

**Case III.**—A. B., a pupil nurse in one of the Philadelphia hospitals, was seen by me at the request of a nose and throat specialist, who thought that it would be advisable for an internist to see her in order to take care of her general condition. She had been sick several days with a decidedly sore throat which on examination was found to be diffusely reddened and slightly edematous but without any evidence of ulceration. The glands in the neck were palpable, as were the axillary glands. Throat smears had been negative for diphtheria and for the organisms of Vincent's angina. A blood count showed that the total leukocytes were 13,600, of which 74 per cent. were classified as lymphocytes. The blood count was repeated every day and gradually, with the subsidence of fever and the disappearance of the anginal symptoms, the leukocytic picture returned to normal.

In this particular instance we have a patient who has one of the types of throat reactions in which there is marked increase in the number of mononuclear cells and, more particularly, of the monocytes. The cells were classified as small lymphocytes and on more careful study it was found that there were a considerable number of them—true monocytes rather than the so-called small lymphocytes.

### III. Leukocytic Response Characterized by Reduction of Total Number of White Cells and Marked Diminution in the Number of Granulocytic Cells, with Marked Constitutional Reaction: Agranulocytic Angina, Aplastic Anemia, and Some Cases of Vincent's Angina.

**Case IV.**—R. P., a negro girl, aged seventeen years, was admitted to the hospital on account of a sore mouth. The soreness of the mouth began ten days before admission. The examination of the patient revealed very little except an ulcerated, bleeding mouth. The mouth smear showed the presence of many fusiform bacilli and spirochetes, but was negative for diphtheria organisms. This young colored woman had a marked anemia. The red cells on admission were 1,240,000. The total white count was 1000; 84 per cent. of these were small mononuclears, 4 per cent. large mononuclears, and 12 per cent. only were apparently young polymorphonuclear cells. The patient on admission to the hospital was extremely sick, with a temperature extremely high, and a rapid pulse rate. Temperature remained high, three days before death averaging 105° F., three examinations on the day of death being 107° F., with corresponding increase in the pulse rate. The total leukocyte count always remained low, with a marked diminution in the number of granulocytes. The oxidase reaction, incidentally, showed that a few cells, which we called polymorphonuclears, did not contain any granules.

**Case V.**—R. C., a white male aged forty-five years was admitted to the ward on account of sore mouth, fever, and weakness which had begun three weeks previously. He had been having chills three days before he noted fever, although of course it is presumably safe to say that he had fever at the same time he had the chills. The fever ran along until one week before he was admitted to the hospital, when he began to suffer with pain on the inside of the left cheek. When the throat was examined this was found to be due to a large ulcer which he told us had spread and was getting worse. When examined in the hospital there was found an ulcerated, necrotic area of the upper left side of the cheek about 2 cm. wide. Except for this finding there was practically nothing to be discovered. On admission to the hospital he was found to have a total number of red cells of 1,380,000. Total white cells were 3500, and the hemoglobin was 30 per cent. The differential count showed small mononuclears 37 per cent., large mononuclears 51 per cent., polymorphonuclears 12 per cent., with marked poikilocytosis and anisocytosis and polychromatophilia. Smears from the mouth showed fusiform bacilli and spirochetes. The other usual laboratory procedures were negative. The man was transfused shortly after he came into the hospital. The total number of red cells rose following transfusion, but the total number of white cells was only 3250, again with a large number of so-called large mononuclears. The man died in five days, all the time having a high temperature. The day before his death the total red cells were 1,410,000, white cells were 1750, hemoglobin was 10 per cent. In this particular case the large mononuclears were really immature forms of granular cells, because the oxidase reaction showed the total number of granular cells averaged between 52 and 60 per cent. On account of the inability to discover any focus of infec-

tion to explain the fever and because of the blood count, despite the higher percentage of granulocytes which were, however, absolutely decreased, the patient was thought to have aplastic anemia and was so diagnosed. The mouth at no time had the frightfully nasty necrotic ulcerative lesions that occur in agranulocytic angina.

### CASES OF VINCENT'S ANGINA

**Case VI.**—C. L., a young negress of twenty-seven years, was admitted to the hospital on account of sore mouth, pains in the head, and weakness. She had the sore mouth for several weeks prior to admission. The explanation of the sore mouth was revealed when the buccal cavity was examined. There was marked salivation. The tongue was red and beefy and along the edges and tip of the tongue were ulcers with a necrotic membrane. The surface of both cheeks was also covered with this necrotic, ulcerative membrane. Beneath the tongue the same condition was present. This patient on admission showed a total red count of 4,250,000, with a hemoglobin of 80 per cent. The white blood-cells numbered 4250 of which 50 per cent. were polymorphonuclears. In this case, then, the white count showed a leukopenia and a polymorphonuclear decrease which was both absolute and relative. The smears from the mouth showed many spirochetes and fusiform bacilli.

**Case VII.**—N. P., a young colored woman aged twenty years, admitted to the hospital on account of sore throat and sore mouth, which she had had for five days. Examination of this young woman's mouth showed the entire buccal membrane reddened and congested. There was a necrotic ulcerative area on the cheek surface near the angle of the jaw and more anteriorly a smaller patch. The tonsils were markedly enlarged and covered with a firmly adhesive membrane. As in the previous case, the examination, except for the local condition, was entirely negative. In neither case were positive cultures gotten for *Bacillus diphtheriæ*. The smears showed many fusiform bacilli and spirochetes. This case showed a low white count. Three days after admission to the hospital her count, which upon admission had been 4500 per cu. mm., had fallen to 4000. Of these 4000 cells, 50 per cent. only were polymorphonuclears, showing both an absolute and relative polymorphonuclear decrease. The mouth condition improved rapidly and the young woman was discharged from the hospital one week after admission.

**Case VIII.**—E. J. was a third case of Vincent's angina in a young colored woman, who was in the hospital for eleven days, gaining admission on account of difficulty in swallowing and swelling of her neck. These acute symptoms she had only noticed for a day and the explanation lay in the greatly congested mucous membrane which showed four or five ulcerated and necrotic areas. Cultures from these areas showed many fusiform bacilli and spirochetes but no diphtheria organisms. Under vigorous treatment the mouth condition improved rapidly. The patient was discharged in apparently excellent condition. This patient also showed a leukopenia, the first count showing 4500 cells and the second count four days later showed 3750 white cells. The differential figures for the first count showed 45 per cent. of small mononuclears, 42 per cent. of polymorphonuclears, and on the second showed 54 per cent.

of small mononuclears, 38 per cent. of polymorphonuclears, the remaining percentage being made up of eosinophils and large mononuclears. This patient also presented the syndrome of Vincent's angina, ulceration of the mouth, many Vincent's organisms present plus a high relative monocyte count and low polymorphonuclear count.

**Case IX.**—S. H., a young Jewish boy, who gave a history of having had diphtheria twice, was admitted with a provisional diagnosis of diphtheria. This was not confirmed, as the organisms were not found in smears or cultures. He did have necrotic ulceration of both tonsils, but his mouth otherwise was negative. Unlike the other cases, the only ulceration was confined to the posterior portion of the mouth. This fourteen-year-old boy had a total count of 8200, but a marked diminution in the number of polymorphonuclears, which had not risen even when the boy was discharged, the highest percentage he had while in the hospital being 30 per cent. He had a high lymphocytic count, averaging between 55 and 60 per cent. He did not exhibit a leukopenia, but he did have a total count which approached more closely the lower than the higher limits of normal and he did have a marked diminution in the number of granulocytes.

**Case X.**—M. R., a three-year-old baby, was admitted to the contagious disease ward on account of a Vincent's angina. No history could be obtained from the child on account of its age and none had been obtained in the admitting room from the parents. This child's mouth showed necrotic areas of ulceration along the gums, and markedly reddened mucous membranes. Cultures from the mouth showed many fusiform bacilli and spirochetes and were negative for diphtheria. This child had a strongly positive Wassermann, and a blood count which was essentially normal except for a rather marked increase in the small mononuclears and diminution in the number of polymorphonuclear cells. After twelve days' treatment the child's mouth condition entirely disappeared. He was transferred to another service for treatment of his congenital lues. It is quite possible in this case that the mouth condition might be explained on the basis of the syphilitic process, but it seems more likely that it was due to the Vincent's angina.

A series of short case histories have here been recorded, namely: agranulocytic angina, aplastic anemia, and many of Vincent's angina. These cases all showed a special blood reaction to their type of throat infection.

### IV. Leukocytosis of High Degree Associated with Marked Increase in the Number of Mononuclear Cells and a Marked Relative Decrease in the Number of Granulocytes.

**Case XI.**—Several years ago I was called to take charge of a small Jewish boy, aged fourteen years, who had a very severe throat infection associated with considerable bleeding of all the mucous membranes of the head, the symptoms of which had been present for only about two weeks. On exam-

ination of this boy's mouth, the whole interior seemed to be gangrenous and sloughing. Cultures from the mouth showed the presence of numerous fusiform bacilli and spirochetes. There was some slight degree of adenopathy but with only a few small, hard, and shot-like, superficial glands, palpable. The blood count in this boy showed the total leukocytes on several examinations to be over 100,000, with the cells of the granulocytic group varying between 2 and 3 per cent. In spite of all treatment the boy rapidly went on to death.

Last year Dr. George Patrick Quinn reported before the student body of Tulane a patient with oral sepsis who had the blood and mouth picture of leukemia. In this particular history the patient had thirteen teeth removed and following this developed a mouth infection. When he was admitted to the hospital it was found that the gums were swollen, spongy, and presented a widespread necrosis and gangrene of the mucous membrane involving the buccal cavity, with the characteristic very foul odor of mouth infections. The patient was found to have marked leukocytosis, 408,000 cells being present in the peripheral blood. Two days later they had risen to 419,000, with 93 per cent. lymphocytes. The cells were classified as an immature form of lymphocytes, lymphoblasts, which was confirmed by the absence of granules in the ectoplasm of the cell when stained by the oxidase method. The patient died the day following this blood-count. In this particular instance they were apparently dealing entirely with a case of acute leukemia of the so-called lymphatic type. I know of no other condition in which there is such an enormous increase of white cells, a fact which would rule out cases with a leukemoid blood-picture, but due to some other cause.

An interesting thing in these 2 cases of leukemia mentioned above is that the acute fulminating symptoms developed concomitant with the mouth infection. In both these instances apparently the condition of the patient was excellent until the mouth infection occurred. It is probably reasonably fair to assume, though this is not by any means definite, that an acute lymphatic leukemia was present prior to the mouth infection, but when this took place very promptly the more spectacular acute symptoms developed.

## SUMMARY AND CONCLUSION

The reaction of the leukopoietic system to various types of throat infection is discussed. These infections may cause, or be associated with, reactions which vary from the ordinary hyperleukocytosis with polymorphonuclear increase to the type found in Schulz's disease, in which there is a marked decrease in the white cells in the peripheral circulation. The frequency with which the ulcerative lesion of Vincent's angina is found in those cases with hypogranulocytosis is stressed. It is suggested that there is a closer relation between the local necrotic process and the blood changes than heretofore was believed possible.

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## GLYCOSURIA

A CONSIDERATION of the subject of glycosuria takes into account, for the purpose of this discussion, the occurrence in the urine of only one of many reducing substances, namely, glucose. Glucose is dextrorotary, is fermented by yeast, and forms osozone crystals with phenylhydrazin.

Glucose occurs in the urine in an amount sufficient to produce reduction of the different copper solutions as a result of one of two conditions: (1) Sugar occurs in the urine when the renal threshold is so low that excretion takes place with the blood-sugar at a normal or subnormal level. In this type of disturbance it is supposed that the cells of the convoluted tubules of the kidney are not able to reabsorb the glucose after its filtration through the glomeruli. As a result of the imperfect functioning of an otherwise physiologically acting kidney, we observe either a constant or an intermittent glycosuria. (2) A disturbance of metabolism occurs which disorganizes the physiologic functions of the various organs, with the result that the body is unable to mobilize, utilize, and store glucose in a normal manner.

It is also possible to conceive of the existence of these two processes in the same individual at the same time, with modifications of the mildness or severity of the one or the other, so that varying degrees or combinations of the two may exist. Perhaps, with further study and more extensive investigation some factors may be found which will determine definitely to which group an individual belongs. Some significance is attached to such a statement by a consideration of the results of investigations recently made by Holst[1] in 11 families in which both diabetic and non-diabetic glycosuria occurred.

One of us (H. M. B.) in studying various members of a very large family has discovered 18 individuals in four generations with glycosuria; one has a mild symptomless diabetes mellitus, the others have an apparently benign glycosuria, some excreting sugar constantly, others intermittently. What is it, therefore, in a given family which determines whether an individual develops a diabetic or a non-diabetic glycosuria? We hope that future investigators will solve this problem.

It has only been within the past decade that the various glycosurias have been separated into different groups. This has been accomplished by utilizing a combined and simultaneous series of observations on patients after the ingestion of sufficient glucose to produce definite changes in the blood-sugar, respiratory quotient, and urinary sugar. As a result of numerous observations made by many investigators, we are permitted to formulate certain ideas concerning the mechanism of the glycosurias, which may be grouped as follows:

A. Patients with glycosuria having a normal or subnormal fasting blood-sugar level, with normal utilization of glucose.
   1. Renal glycosuria.
   2. Cyclic renal glycosuria, or alimentary glycosuria.

B. Patients with glycosuria, having a normal fasting blood-sugar level, but with an inability to readily mobilize and store increased doses of glucose.
   Diabetes innocens.

C. Patients with glycosuria having a normal or an increased fasting blood-sugar level and an inability to normally utilize, mobilize, and store glucose.
   Diabetes mellitus.

Practically all patients who have sugar in their urine may be placed in one of these three groups. A discussion of some of the factors involved in the production of these various types of glycosuria will be given as each condition is brought to your attention.

1. **Renal Glycosuria.**—This condition is characterized by the constant presence of glucose in the urine; the blood-sugar does

not exceed a normal postabsorptive level after the administration of glucose; the body metabolizes and stores glucose in a normal way; there are no symptoms of diabetes mellitus and patients with this condition, observed over a long period of time, do not develop diabetes. The following case is illustrative and probably represents the youngest case reported.

C-4094, K. D., white female, age three years, first seen May 12, 1924. She was a full term, normally delivered baby weighing 7½ pounds at birth. When twelve days old she had projectile vomiting which was relieved almost entirely by taking "drops" three times daily. She was breast fed until seven months when she was put on "malt soup, milk combination," which she took until eighteen months old. At this time other foods were added in appreciable quantities. At one year of age she weighed 9 pounds. She sat alone at six months, began to say words at nine months, and talked at one year. She has never walked. The appetite has always been poor. She has never seemed thirsty, although her mother thinks that she has always passed a good deal of urine. She voids now about every hour during the day, and the twenty-four-hour output is very nearly 1 quart. March 1, 1924 she weighed 21 pounds. Sugar was discovered in the urine April 4, 1923 when two years of age. Beyond moderate restriction of carbohydrate no other dietary regulation was attempted. Since the first discovery of sugar the urine has never been free of sugar. There is no history of diabetes in the family.

*Physical Examination.*—The patient is a poorly developed, undernourished child, weighing 8.2 kg. and 72.5 cm. tall. She is unable to stand alone because of muscular weakness of the lower extremities. Mentally she is quite alert and responsive. The general physical findings reveal very little of importance except the gross signs of rickets: a protuberant abdomen, and a liver extending 3 cm. below the costal border without enlargement of the spleen and without fluid in the peritoneal cavity. The extremities are quite flabby and there is no evidence of paralysis or disturbance of sensation. There is no edema. The superficial and deep reflexes are present and equal. Observations concerning this patient are contained in Table 1 (page 1394).

The points of interest are:

(*a*) With dietary restriction, limiting the total glucose of the daily intake to approximately 70 gm. there is an almost constant amount of sugar excreted in the urine.

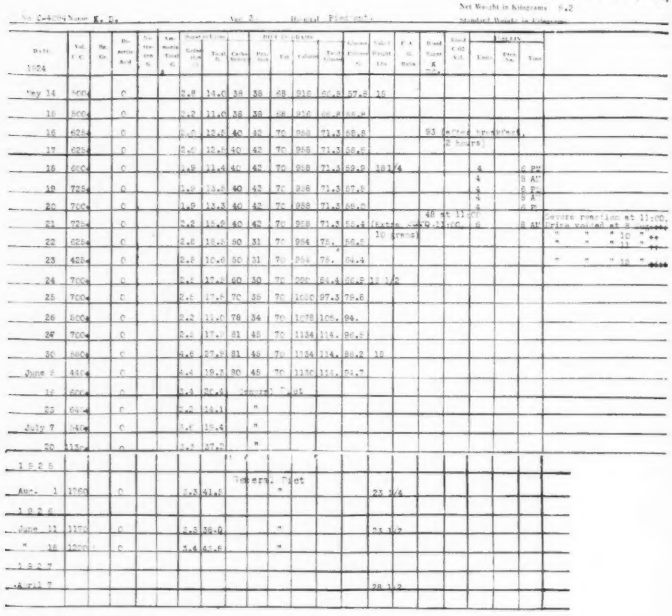
(*b*) With increase in the daily amount of total glucose in the diet there is an increased amount of sugar excreted in the urine, not equal however to the increase in supply.

(*c*) The blood-sugar two hours after a breakfast, containing approximately 20 gm. of glucose, was only 93 mg.

(*d*) The administration of 4 units of insulin twice daily did not appreciably decrease the amount of sugar excreted in the urine.

(*e*) The production of insulin shock, with a blood-sugar of 48 mg. did not free the urine of sugar at the beginning or at the height of the shock.

TABLE 1



(*f*) With no dietary control—after one month of restricted diet—the patient, during a period of three years, has not had any symptoms of diabetes. Neither has there been any evidence of acidosis.

(*g*) It is possible that the constant loss of glucose in the urine might have influenced the retarded physical development of this patient.

(*h*) Because of the age of the patient it was impossible to make metabolic studies.

The evidence presented classifies this patient as belonging to a well-recognized group of individuals who constantly excrete sugar in the urine and have a fasting blood-sugar level which is either normal or subnormal. During a glucose tolerance test, in which 50 or 100 gm. of glucose dissolved in 300 c.c of water with the juice of one lemon is given on a fasting stomach —the majority of these patients respond with a practically normal blood-sugar curve, and a varying glycosuria, the extent of

each depending measurably upon the renal threshold for sugar. Those patients having a low threshold excrete sugar in large amounts and over a longer period of time than those who have a threshold at a more nearly normal level. These patients are otherwise able to store, mobilize, and utilize glucose just as a normal individual.[2]

2. **Cyclic Renal Glycosuria or Alimentary Glycosuria.**—As ordinarily interpreted this is understood to mean that a perfectly normal individual may excrete sugar in the urine after taking normal or increased amounts of dextrose or carbohydrate-containing foods at meals. The difference between this type of patient and the true renal glycosuric is probably more of degree than anything else and depends, in some measure at least, upon the difference in the renal threshold in the two classes of cases. This type of patient does not eliminate sugar constantly in the urine, but sugar is most always found after a meal containing the usual or an increased amount of carbohydrate. Sugar excretion may be present for several hours and then the urine may remain sugar-free the remainder of the day. After a sugar tolerance test the blood-sugar curve usually rises to a level of 140 to 160 mg. per 100 c.c. and returns to the fasting level within two hours. As the blood-sugar concentration reaches a certain level (between 120 and 140 mg.) which is constant for these individuals, sugar begins to spill over in the urine and continues to do so until the sugar in the blood returns to a concentration below the level at which sugar first appeared in the urine. The patient otherwise mobilizes, utilizes, and stores glucose as a normal individual.

Another group of individuals which has been classified by some authors as cyclic renal glycosuria demands more study and more attention. Just what the mechanism of the glycosuria is in these cases has not been satisfactorily explained. I refer to the individual who shows sugar in the urine after an ordinary meal, and a sugar-free urine after a night's fast. The fasting blood-sugar is normal. After the administration of 100 grams of glucose there is a marked hyperglycemia (the peak reaching 210 to 240 mg.) which is sustained over a period of three or four hours

before returning to the normal level. Some evidence has been presented by Holst,[3] Faber,[4] Malmros,[5] and others that cases of this type differ from mild diabetes. The points of differentiation are not clear, but when these patients are observed over a long period of time they do not develop symptoms of diabetes. Stress is laid upon the fact that most of these patients have a normal fasting blood-sugar; this is of great importance in differentiating between the benign type of glycosuria and mild diabetes. At present we are justified in admitting the existence of this condition, but patients so classified should be closely observed over a period of years. If a group of such patients could be studied during the progress of an acute infection valuable information could be obtained concerning the behavior of the blood and urinary sugars. As a result of the altered metabolism one could determine the similarity or non-similarity to diabetic behavior.

3. **Diabetes Innocens.**—This term is applied to an unusual clinical condition which shows certain characteristics of diabetes mellitus, but apparently runs a harmless course. Such cases have been described by Salomon,[6] Frank,[7] and Riesman.[8] Not all of their cases are easily classified since no detailed observations were made on the blood-sugar after the ingestion of glucose or food.

Campbell[9] emphasizes the following points in the differentiation of diabetes innocens from diabetes mellitus: The discovery of glycosuria is accidental. There are no symptoms of diabetes except glycosuria, and such symptoms do not occur despite the long duration of the condition and absence of dietary regulation. Sugar is present in the urine with normal fasting and postprandial blood-sugar levels. There is an increase in glycosuria with increased carbohydrate intake, but the increase is not commensurate with the increase in food. Respiration studies show high respiratory quotients, demonstrating carbohydrate utilization and other features incompatible with the diagnosis of mild diabetes.

Parsons[10] gives a detailed report and the results of metabolic studies in a woman who had shown glycosuria for nine years and

had been under observation and diabetic management for four years. The clinical course of this patient corresponds to the description given by Campbell.

Vogelenzang[11] reports 2 cases under the title "Combination of Diabetes Mellitus and Renal Glycosuria." Both patients were adult males. The resemblance to renal glycosuria was seen in the absence of diabetic symptoms and the occurrence of glycosuria, accompanying a normal or low blood-sugar level. At the same time a resemblance to diabetes mellitus was noted in the following facts: Following glucose ingestion the blood-sugar level exceeded the normal figure and remained elevated too long; accompanying increased food intake there was an increase in glucose excretion in the urine. The author was unable to find any report of similar conditions in medical literature. He ascribed the harmless course of the condition in both patients to the low renal threshold which precluded the possibility of a high glycemic level being maintained. The following case is illustrative.

C-6066, a male, single, aged forty-seven years, was seen May 20, 1927; his complaint was diabetes. There was no history of diabetes in the family. He had had the usual diseases of childhood, typhoid fever and gonorrhea during 1901, and malaria during 1917. Appendectomy had been performed during 1921. He had always been constipated. His greatest weight had been 172 pounds, shortly after the appendectomy; his average weight had been 160 pounds.

During the spring of 1923 the patient began to notice marked fatigue at the end of his day's work at farming. He consulted several physicians without obtaining relief; he does not think that his urine was examined. During November, 1924 he consulted an internist who found sugar in his urine and made a diagnosis of diabetes; he weighed 158 pounds at this time. A rough restriction of diet was instituted, accompanied by 10 units of insulin twice daily. He adhered to his diet rather faithfully, but made occasional changes in his insulin dosage. He states that his urine was never sugar free. He had never experienced the usual diabetic symptoms of excessive appetite, thirst, increased frequency of urination, or nocturia.

*Physical Examination.*—His height was 5 feet, 11½ inches; his naked weight was 128 pounds. The radial vessels were easily palpable and slightly thickened. His blood-pressure was 100 systolic, and 66 diastolic. The remainder of the examination revealed no abnormal findings.

A casual specimen of urine produced a marked reduction of Benedict's solution; diacetic acid was not present. There was a faint trace of albumin

and rarely a hyaline cast. The urine was dextrorotary and fermented with yeast. Crystals were formed with phenylhydrazin. Seliwanoff's test for levulose was negative. The hemoglobin, red blood-cell and white blood-cell counts, and differential white-cell count were within normal limits. The blood Wassermann was negative. The fasting blood-sugar was 114 mg. per 100 c.c. of blood.

The patient was placed on a diet of carbohydrates, 80 grams; protein, 80 grams; and fat, 180 grams; accompanied by insulin, 15 units in the morning and 10 units in the evening. Tests of separate voidings carried out for thirty-six hours showed a sugar-free urine in only one specimen on this diet and insulin dosage. (He had remained in the hospital several days on this regime without becoming sugar-free when he found it necessary to return home.)

He returned for further study July 19, 1927, stating that he had adhered to the above diet and insulin dosage for seven weeks without becoming sugar-free or gaining in strength. His naked weight was 129¾ pounds. His fasting blood-sugar was 102 mg. per 100 c.c. of blood. On a diet of carbohydrate, 75 grams, protein 80 grams, fat 170 grams, and 25 units of insulin daily for a period of two days, his average glucose excretion was 11.5 grams, or 8.3 per cent. of the available glucose in the diet. While receiving this diet and insulin dosage, nine single specimens of urine were tested during twenty-four hours, and all of these showed sugar.

On July 29th 100 grams of glucose were given by mouth as lemonade, with the following results:

| 7–20–27. | Blood-sugar. Per cent. | Urine-sugar. Per cent. | Urine-sugar. Grams. |
|---|---|---|---|
| Fasting | 0.112 | 0.7 | 1.75 |
| Glucose, 100 grams by mouth | | | |
| 20 minutes later | 0.190 | | |
| 40 minutes later | 0.230 | 2.8 | 2.52 |
| 1 hour later | 0.290 | 2.0 | 2.3 |
| 2 hours later | 0.175 | 1.7 | 7.6 |

On August 2nd before breakfast his blood-sugar level was 101 mg. An inlying urethral catheter had been fastened in the bladder and 222 c.c. of urine containing 0.7 per cent. of sugar had been removed at the time of collection of the blood specimen. Forty units of insulin was injected subcutaneously. The bladder was irrigated at intervals with sterile saline solution. Water was taken in large quantities by mouth. The bladder was emptied every two or three minutes, and the separate specimens of urine were tested with Benedict's solution. In one hour and twenty-five minutes the bladder-urine became sugar-free for the first time; the simultaneous blood-sugar level was 73 mg. There were no symptoms of an hypoglycemic reaction. Within one minute the patient took 100 grams of glucose by mouth as lemonade and the testing of urine specimens was continued. Sixteen minutes after the ingestion of glucose Benedict's solution again showed definite presence of sugar in the urine; the simultaneous blood-sugar level was 120 mg.

August 3rd simultaneous blood and urine specimens were collected one

hour and forty-five minutes after breakfast. The blood-sugar reading was 0.158 per cent., and 500 c.c. of urine contained 1.7 per cent. sugar.

The patient returned home August 3rd with a naked weight of 131½ pounds. He was advised to avoid sugar and sweets, but was permitted to take a somewhat limited amount of all other carbohydrate foods; no other restriction of diet was advised and no insulin was taken.

He returned October 4th, two months later, with a naked weight of 146 pounds. He reported that he had regained his strength, was feeling greatly improved, and had had no diabetic symptoms except glycosuria. Simultaneous blood and urine specimens were obtained four hours and ten minutes after his noon meal. The blood-sugar reading was 105 mg. and the urine contained 1.3 per cent. glucose.

The next day a second glucose tolerance curve was plotted after administering 100 grams of glucose by mouth.

| 10–5–27. | Blood-sugar. Per cent. | Urine-sugar. Per cent. | Urine-sugar Grams. |
|---|---|---|---|
| Fasting | 0.116 | 1.6 | 1.2 |
| Glucose, 100 grams by mouth: | | | |
| 1 hour later | 0.317 | 2.7 | 3.5 |
| 3 hours later | 0.175 | | |
| 3¾ hours later | | 1.0 | 0.6 |

About fifteen minutes before the three-hour blood-sugar specimen was obtained the patient complained of extreme hunger and weakness; his expression became anxious and he broke out in a profuse drenching sweat. His pulse rate was elevated to 92 per minute. He was unable to void at the three-hour interval. He was then given about 40 grams of glucose by mouth, resulting in prompt relief of his hypoglycemic symptoms.

December 6th his naked weight was 153½ pounds, representing a gain of 24½ pounds since discontinuing his restricted diet and insulin 4½ months previously. A twenty-four-hour specimen of urine, volume 3200 c.c., contained 1.8 per cent. sugar and no diacetic acid. Simultaneous blood and urine specimens were collected one and one-half hours after a meal; the blood-sugar reading was 154 mg. and the urine contained 3.1 per cent. of sugar. The following day the blood-sugar was 112 mg. three and one-half hours after a meal. The effect of increasing the total carbohydrate of the diet was tried according to Table No. 2 on page 1400.

It is observed that during a period of four days with a total available glucose intake of 596 grams, 18.5 per cent. of this was excreted in the urine. With an increase of the total glucose intake to 1027 grams only 11.9 per cent. of this was excreted in the urine.

The points of interest are:

(*a*) A patient forty-seven years old with a marked glycosuria known to have existed for over three years unaccompanied by any symptoms of diabetes except weakness and loss of weight, these probably due to the imposed dietary restriction rather than any ill-effect of the disease.

(*b*) Blood-sugar levels were always within normal limits in the fasting state and after the ingestion of food.

(*c*) The urine always contained sugar but no acid bodies.

(*d*) While receiving weighed diets the amount of glucose excreted in the

TABLE 2

| Date, 1928. | Naked weight, pounds. | DIET | | | | | URINE | | | Blood Sugar, Per Cent Fasting. | SUMMARY | | | Response to graded diets of increasing carbohydrate content and approximately isocaloric value. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Carbohydrate, Grams. | Protein, Grams. | Fat, Grams. | Calories | Available Glucose, Grams. | Volume, c.c. | Glucose in Urine: Reduction Per Cent. | Glucose in Urine: Total Grms. | | Total available glucose each diet period, grams. | Total glucose excretion each diet period, grms. | Percent total available glucose excreted each diet period | |
| 8-14 | | 100 | 63.0 | 150 | 2002 | 151.6 | 2575 | 0.95 | 24.5 | 0.070 | | | | |
| 8-15 | | 100 | 63.0 | 150 | 2002 | 151.6 | 3005 | 0.76 | 22.7 | | | | | |
| 8-16 | | 91 | 61.5 | 150 | 1960 | 141.7 | 1465 | 1.85 | 27.1 | | | | | |
| 8-17 | | 100 | 63.0 | 150 | 2002 | 151.6 | 3620 | 1.00 | 36.2 | | 596.2 | 110.8 | 18.5 | |
| 8-18 | | 100 | 61.5 | 116 | 1930 | 207.3 | 4075 | 0.79 | 32.3 | | | | | |
| 8-19 | 147 | 160 | 61.5 | 116 | 1930 | 207.3 | 3335 | 0.84 | 28.0 | | | | | |
| 8-20 | 147 1/2 | 140 | 61.5 | 116 | 1850 | 187.3 | 2980 | 1.18 | 34.7 | | 601.9 | 95.0 | 15.8 | |
| 8-21 | 148 1/4 | 230 | 60.5 | 90 | 1972 | 274.0 | 2325 | 1.00 | 23.2 | | | | | |
| 8-22 | 148 1/4 | 230 | 60.5 | 90 | 1972 | 274.0 | 2940 | 1.33 | 39.2 | | | | | |
| 8-23 | 150 1/4 | 220 | 62.5 | 90 | 1940 | 265.2 | 2685 | 1.45 | 41.4 | | 813.2 | 103.8 | 12.8 | |
| 8-24 | 150 | 300 | 61.5 | 67 | 2049 | 342.3 | 3800 | 1.11 | 42.2 | | | | | |
| 8-25 | 149 3/4 | 300 | 61.5 | 67 | 2049 | 342.3 | 3355 | 1.20 | 40.4 | | | | | |
| 8-26 | 150 | 300 | 61.5 | 67 | 2049 | 342.3 | 3000 | 1.35 | 39.5 | 0.085 | 1026.9 | 122.1 | 11.9 | |

urine was only slightly increased by raising the carbohydrate intake of the food.

(*e*) With increases in the available glucose intake there was a decrease in the percentage of the available glucose excreted.

(*f*) Glucose tolerance curves show an hyperglycemia at the end of one hour, such as is observed in diabetics; the hyperglycemia is more prolonged than a normal response to the ingestion of glucose.

(*g*) Spontaneous hypoglycemia occurred three hours after the last glucose tolerance test which we assume is very good evidence that the pancreas is able to supply a good quality and quantity of insulin.

(*h*) The renal threshold in this patient is quite low. During the period of observation his urine was never sugar-free, even with a low blood-sugar level, or when insulin was given in an effort to promote better carbohydrate utilization. The renal threshold, even when roughly tested by the method we have described, resembles in all respects that of renal glycosuria. The variation in the blood-sugar level at which the urine ceased to show sugar and again contained sugar is in keeping with observations by others in this condition.

4. **Diabetes Mellitus.**—It is unnecessary to say much concerning this condition. Everyone is familiar with the many and extensive studies which have been made on patients with diabetes mellitus and on animals with partial and complete pancreatectomies. In the diabetic patient there is a disturbance of

the carbohydrate metabolism due to a deficient supply of insulin, or the supply is of inferior quality. This deficiency prevents the proper storage of glucose in the liver and muscular system so that there is an increase in the sugar content of the blood. The body is unable to properly burn carbohydrate so that the entire metabolism of protein and fats suffers and there results, in many cases, acidosis or the accumulation in the body of unoxidized fatty acids. The body is unable to mobilize, store, and utilize the supply of glucose. Consequently, the excess is excreted in the urine.

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CLINIC OF DR. PAUL H. RINGER

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## THE PROBLEM OF COLLAPSE THERAPY IN PULMONARY TUBERCULOSIS

THE problem of collapse therapy is the great one confronting all interested in restoring those suffering from pulmonary tuberculosis to a state of working efficiency; that is to say, to a state of "economic recovery."

The factors in the treatment of tuberculosis are social, economic, philanthropic, medical, and surgical. With the first three factors we are not here concerned. The fourth resolves itself largely into *bed rest*, coupled with full feeding and followed after many months by carefully graduated exercise; this treatment to be followed preferably in an institution; if this is not practicable, in the home.

It is with the fifth factor, that of surgical treatment or collapse therapy (including artificial pneumothorax), it is proposed to deal. The literature on this rather highly specialized phase of treatment is voluminous—as a matter of fact quite too voluminous, but it is decidedly restricted to the special journals in the various languages, and the man doing general medicine sees but little of it. Alexander's "Surgery of Pulmonary Tuberculosis" is a concentrated masterpiece and should be of absorbing interest to every medical man: yet many will fail to buy it, thinking it too technical and restricted for their purpose.

It has been thought that a brief review of collapse therapy, appearing in a journal wholly undevoted to specialties, might be of use to the man who sees tuberculosis only as he sees many other diseases, in the routine of general practice.

Sanatorium and hygienic-dietetic treatment of tuberculosis is efficient and sound, but to many individuals it is out of the question because of lack of money. It is a sad fact that a multitude of the tuberculous "cannot afford to get well." Recovery from definite pulmonary tuberculosis, by which is meant definite physical signs, definite *x*-ray findings, and definite symptoms, cannot possibly occur under one year, and in the vast majority of open cases, this time is doubled and frequently trebled or quadrupled. The man or woman of moderate means, face to face with an economically unproductive period of one to four years, runs up against an "impasse." The patient, as above stated, "cannot afford to get well."

Collapse therapy, in addition to being a potent factor in diminishing symptoms, in lessening poison absorption, and in bettering the clinical condition of the patient, is a great "short-cut" to recovery. Anything that reduces the time necessary to recovery from pulmonary tuberculosis is of inestimable advantage to the patient, for it is the attrition of the disease rather than the disease itself, that wears down many.

The basis of all collapse therapy is of course rest to the diseased organ. Rest is looked upon as the cornerstone of treatment in tuberculosis, yet the damaged lung moves from eighteen to twenty-four times per minute in its respiratory excursions. The whole problem of collapse therapy rests upon lung immobilization.

What, then, are the indications? They may be very briefly stated.

1. Unilateral active disease, especially if there is evidence of cavity formation.

2. Bilateral disease where by physical and *x*-ray examinations there is no activity in the process of the less involved lung.

Cases presenting equal or approximately equal bilateral involvement are unsuited for collapse therapy. Certain selected cases can be subjected to modified collapse therapy on both sides, but these cases are wholly within the domain of the expert and have no place in this discussion. There are certain contra-

indications to collapse therapy. The following are usually named:

1. Active disease in relatively sound or contralateral lung.
2. Laryngeal tuberculosis.
3. Tuberculous enteritis.
4. Advanced nephritis.
5. Diabetes mellitus.
6. Tuberculous meningitis.

The writer is certain that laryngeal tuberculosis unless very advanced is no contra indication, and is also of the opinion that in relatively mild cases of tuberculous enteritis collapse therapy can be used to good advantage. Of course the decision depends essentially upon two factors: (*a*) The degree of the complication, and (*b*) the type of collapse therapy that can be utilized for obviously one would proceed fearlessly with the induction of an artificial pneumothorax where one would recoil absolutely from an extrapleural thoracoplasty.

The time has come when the internist familiar with the pathologic changes found in pulmonary tuberculosis, and with their extent, should be able to outline to the patient what lies ahead of him, what can and cannot be done, and what results may be and may not be expected.

It must here be emphasized that unilateral cavity formation is one great indication for collapse therapy. Rapidly spreading exudative processes are also conditions in which this procedure is employed. These latter, however, under rest in bed for many months, often show a remarkable absorption of pathologic deposit, and it must be remembered that lesions of the fibroid productive type yield better to collapse therapy than the acute exudation processes. Cavity formation is always nature's last endeavor to stem the tide. Therein she breaks her dykes to save herself, and when extensive cavitation is present it is obvious that the natural forces of resistance have their backs to the wall. Furthermore, cavity formation is a predisponent to hemoptysis, and it is too well known how serious a complication is hemorrhage in individuals with large cavities. The patient with excavation present is veritably walking on

a mine which may at any moment explode and bury him beneath the débris of exsanguination, general dissemination of the disease process, or tuberculous pneumonia.

Thus forewarned, what procedure comes naturally to the mind of the attending physician? Artificial pneumothorax. In those cases in which it is successfully and completely induced the result is such as to constitute veritably one of the miracles of modern medicine. There is no more dramatic change in the clinical condition of an acutely ill tuberculous individual than that brought about by a complete unilateral lung compression. The abrupt fall in temperature, the lessening and disappearance of cough and sputum, the improvement in the general sense of well-being, the gain in weight and strength: all these arriving concurrently, seem to constitute a veritable magic of therapy.

But this is the ideal case! And in too many this ideal is not realized. To be sure, in the large majority of those in whom a workable artificial pneumothorax is obtained there is seen marked improvement *up to a certain point:* and at that point, the patient remains stationary. Cough and sputum have been appreciably reduced. Fever has disappeared. Weight has been gained, and therewith strength. The patient is clinically better, but the patient is not clinically well, and as time passes by both patient and physician become weary of the incessant "marking time." A life may have been saved, but an economic recovery is far from being achieved.

Why is this? It is because a partial but not a total pulmonary compression has been obtained. Various areas of parenchymal involvement have ceased to function as active foci, but the seat of the trouble, the cavity, or cavities, have, because of the presence of parietal pleural adhesions, proved incapable of compression. Fairly high air-pressures may be tried in the hope (usually vain) of breaking an adhesion. Very high pressures are risky because of the fact that if an adhesion should give way there is no guaranty on which end it will yield, and, should it be on the pulmonary end, tearing of lung tissue with resultant spontaneous pneumothorax, infection, pyopneumothorax, and all its melancholy train of

symptoms would ensue. We place ourselves definitely on record as opposed to very high manometric pressures.

It would seem, therefore, that given a partial pneumothorax, maintained for some months and proving unchangeable, *i. e.*, one with considerable compression of pulmonary parenchyma, but lack of compression of one or more cavities, the maximum therapeutic effect of the procedure has been attained and nothing further remains to be done.

Up to within a very few years this was actually the case, save for those patients who had at their command both the moral and physical courage on the one hand, and the expert surgical advice and skill on the other, to venture with the stormy field of extrapleural thoracoplasty—of which more later.

So many cases of partial pneumothorax presented themselves that surgical thought and effort were directed toward rendering these partial compressions total, without resorting at once to the most radical measures. Thus, there was borrowed directly from the thoracoplastic field the minor and preliminary operation of phrenicotomy or, as it is better named, phrenico-exeresis, whereby, as a result of a relatively simple surgical intervention (save insofar as a very accurate anatomic knowledge of neck-dissection is involved) the phrenic nerve on the involved side is exposed and avulsed with resultant paralysis of the corresponding leaf of the diaphragm and a rise of its dome from 3 to 11 cm. which, coupled with permanent immobility, aids in lung compression. It has been estimated that a successful phrenico-exeresis brings about approximately one-third to one-fourth as much pulmonary compression as does a completely successful artificial pneumothorax. Of course the greatest benefit from phrenico-exeresis is to be found in those cases having lower lobe lesions; yet, the mechanics of pressure and of relief of tension within the pleural cavity are at best uncertain, and frequently even in upper lobe involvement, paralysis of the diaphragm will result in relief of tension on an adhesion to such an extent that the walls of a hitherto incompressible cavity will coaptate and obliteration of the destructive lesion will result.

The operation is done under local anesthesia and is a com-

paratively simple one for the surgeon with an accurate knowledge of the triangles of the neck. It must be borne in mind, however, that there are several anatomic aberrations possible on the part of the phrenic nerve, and the surgeon about to undertake this procedure should familiarize himself with them in order not to be dismayed if, upon exposure of the anterior surface of the scalenus anticus muscle the nerve is not at once plainly seen.

Still another method can be employed for converting partial into total compression. Professor Jacobaeus, of Sweden, in 1913, devised a method of severing string or band-like adhesions that acted as guy-ropes to keep cavities from collapsing. By means of an electrically-lighted tube analogous to a cystoscope, and called a thoracoscope, he directly investigated these adhesions and, when deemed suitable, he severed them by introducing through a separate opening in the pleural cavity an electrocautery by means of which, when heated to a dull-red, he slowly seared the adhesion until it gave way and the wall of the cavity was no longer subject to traction and could, therefore, collapse. It was found that adhesions thus directly explored frequently presented a very different appearance from that viewed in the *x*-ray film, for while in the latter they could be seen but in one plane, upon investigation with the thoracoscope linear appearing adhesions were found to be broad and band-like and other differences not demonstrated roentgenologically were apparent, while, in addition, many adhesions were seen which had been invisible on the *x*-ray film. Cases, therefore, which from the *x*-ray picture appear wholly suitable for this procedure, upon thoracoscopic examination may be found impracticable for its application. Thick band-like adhesions above the third rib are almost uniformly unsuitable for cauterization. The method is not without its dangers. Cauterization must be done slowly and with the cautery at only a dull-red heat in order to sear the blood-vessels that will be encountered in the adhesions. Bright red or white heat will too rapidly burn through the vessels and will predispose to hemorrhage. It is of paramount importance to let the cautery under no circumstances penetrate the wall of a cavity, as then a spontaneous pneumothorax is brought about with its train of infection, tuberculous empyema,

and all the sad effects which follow. In the properly selected case, with satisfactory technic, this method bids fair to become far more widely used than it is at present. In this country the outstanding worker in this field is Ralph C. Matson of Portland, Oregon, who has achieved excellent results.

Pneumothorax being but partially successful, phrenicotomy or phrenico-exeresis being insufficient, and cauterization of adhesions impracticable or unsatisfactory, what remains to be done in order to secure pulmonary collapse? Extrapleural thoracoplasty. This operation developed most fully by Wilms and Sauerbruch, in Germany, consists in the excision of portions of the ribs, beginning with the first and extending to the eleventh. In all, in a complete thoracoplasty, about 120 cm. of ribs is removed. The shortest piece of rib removed is that portion taken from the first rib, which is also the most difficult part of the entire operation and incidentally the key to its success. As progression is made downward larger and larger sections of rib are removed. By this procedure collapse of the lung is insured and obliteration of cavities is rendered most probable, although this does not always occur even at the hands of those most skilled. Extrapleural thoracoplasty is a serious operation and postoperative shock and pain are sometimes severe and prolonged. The results, however, are so good that the procedure is wholly justifiable. In a review of over 1000 cases of thoracoplasty Sauerbruch states that "less than 4 per cent. came to an early end. In favorable cases, only 1 to 2 per cent. died. Lasting cure resulted in 42 per cent., and improvement in 40 per cent." Authorities differ as to the method to be adopted in its performance. Today but few advocate doing the entire operation at one fell swoop, feeling that the shock is too great. Most surgeons favor a two-stage operation, the upper ribs (four or five in number) being removed at the first operation and the lower ones at a second operation performed as soon after the first as the patient's condition permits, preferably within three weeks, in order that fixation of tissues in their new position may not become too great.

Dr. Hedblom of Chicago has concluded from his wide experience that patients do better if the operation is done in

three, four, or even five stages, as postoperative shock is thus lessened.

The actual operative mortality of this procedure in the hands of skilled men, is not great and the results are on the whole satisfactory. A complete thoracoplasty is by no means always necessary. With an apical lesion a partial thoracoplasty can be done, involving the number of ribs that must be sacrificed in order to obliterate the lesion. When preceded by phrenico-exeresis, frequently the partial compression so obtained is sufficient to reduce the extent of major surgical intervention.

To recapitulate then, the ideal form of collapse therapy is artificial pneumothorax. Simple to induce, practically painless, almost wholly free of danger and, when complete, the most productive of clinical results, it stands today an enduring monument to its originator, Carlo Forlanini of Pavia.

If artificial pneumothorax is found to be wholly inapplicable, then of course the Jacobaeus method of adhesion-cauterization is out of the question, as it can only be employed when a partial pneumothorax exists. The two operations of phrenico-exeresis and of extrapleural thoracoplasty remain. In cases with a definitely thickened pleura over the lower lobe of the affected side, with evidences of thick strong pleural adhesions, it is very doubtful whether phrenico-exeresis will produce sufficient rise in the dome of the diaphragm to warrant its performance. In such cases it is best to proceed at once with the thoracoplasty. It has been said that a good pneumothorax is better than a thoracoplasty, but that a good thoracoplasty is better than a bad pneumothorax (Claus).

The cases requiring nicety of judgment are those in which a partial pneumothorax has been obtainable. No two cases are alike, and each must be judged on its own merits. The surgeon that is interested in collapse therapy must have a good knowledge of pulmonary tuberculosis, and the physician that is interested in pulmonary tuberculosis must have a general acquaintance with the various methods of surgical intervention, what they seek to attain, how they seek to attain it, what risk is involved, what limitations present themselves, and what in-

dications and contraindications are present with regard to the various procedures. The physician should always be present at every operative interference upon his patient (this applies not only to the subject under discussion, but to all surgical procedures as well) and the surgeon, even after his active work is done, should maintain contact with the patient in order to be able to appreciate and to evaluate his end-result, which is, after all, the most important point in the whole matter.

Finally, though the tenor of this article is decidedly in favor of collapse therapy, a word of warning must be sounded as regards its over-use. There are some who would rush every unilateral case of pulmonary tuberculosis to the pneumothorax table and, failing there, to the operating room for one of the more drastic surgical procedures that have been discussed. With this radical view the writer finds himself at variance.

The elimination of one lung from performing its physiologic function is a radical procedure and must always be recognized as such. While wholly justifiable and definitely indicated in many, many cases, it should not supplant or eliminate the time-tried and well-tested tripod of Rest, Fresh air, Good Food.

Collapse therapy is an *aid* to recovery from pulmonary tuberculosis and no more takes the place of the basic principles of the "cure" than does insulin take the place of carefully regulated and balanced diet in diabetes mellitus.

In the enthusiasm which the results of successful collapse therapy in whatever form have engendered, the natural healing forces of the body, those elements leading to fibrosis on the one hand and to absorption of exudate on the other, in short, that often-used and vaguely mystical word "resistance" must not be lost sight of. What "resistance" really is, we do not know, and yet it is upon its presence or absence that is based recovery or death. While ignorant of its nature and mode of action, we can estimate its potency in any given case not by the physical or roentgenologic evidences of disease, but by the clinical symptoms presented. Evidence of toxicity is a far greater indication for collapse therapy in the anatomically suitable case than is mere cavity formation. It must always be remembered that

while collapse therapy, particularly in its more drastic surgical forms has been with us rather less than twenty years, cavities have been healing spontaneously since Mosaic times, and that while the mechanics of civilization have changed tremendously, the mechanics of the healing of a pathologic process are today the same as they were in the age of King Tut.

So let us weigh everything carefully. We have today methods at our command which are invaluable in aiding a diseased lung upon its way to cicatrization. We have the same age-old natural processes that have effected so many recoveries throughout the centuries. Both elements must be kept in mind, those under the control of man and those under the control of nature, and the method of procedure must be decided upon after a careful estimation of the value of each as expressed in the condition of the patient. Too great enthusiasm will lead us on the rocks of meddlesome surgery; too great conservatism will make us responsible for the loss of valuable lives that might and should have been indefinitely prolonged. Ours is the choice for better or for worse. Hippocrates summed it all up in his famous aphorism:

> "Life is short, and the Art long; the occasion fleeting; experience fallacious, and judgment difficult."

## CLINIC OF DR. STEWART R. ROBERTS

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# NEUROPATHIC DROPSY OF THE RIGHT FOREARM AND HAND

MISS F. W., aged sixteen years, a school girl, was seen November 19, 1928. She had complained of swelling and pain in the right hand and forearm for a year. Her father died of chronic alcoholism and her mother of pulmonary tuberculosis, both at thirty-five years of age. One brother was well at the age of twelve. In September, 1927 she complained of pain in the right wrist

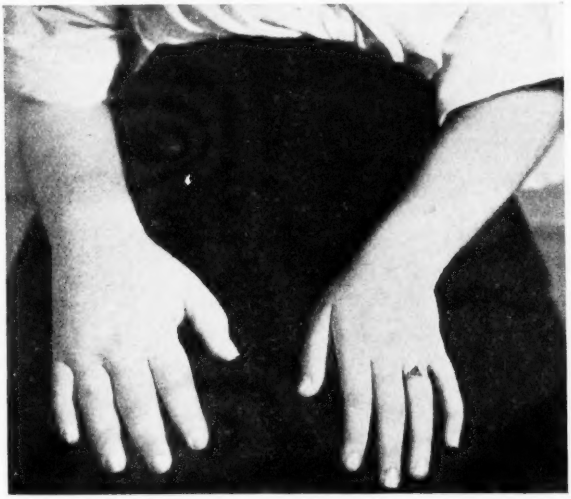

Fig. 221.—Appearance of the right hand before treatment. Note the swollen right hand compared with the normal left (November 1, 1928).

joint which was followed in a few days by swelling which involved the joint and gradually increased until in two weeks the entire hand and forearm were edematous. It was a typical pitting dropsy. The edema lasted three months, that is, until December, 1927, and gradually disappeared. The hands seemed normal. In January, 1928 pain developed in the left hip-

joint until finally she was compelled to go to bed. Pain and tenderness were marked, but there was no edema anywhere nor did the *x*-ray reveal any bone pathology. She was in bed for six weeks, on crutches for six weeks, and by May seemed well. In June, 1928 she complained again of pain in the

Fig. 222.—Lateral view showing the ham-like right hand and swollen lower half of right forearm (November 1, 1928).

Fig. 223.—Hand after treatment on discharge of patient from hospital (December 18, 1928).

right wrist followed in a week by swelling of the entire hand and forearm. There was much pain and tenderness, particularly on use. From June to November, 1928 there was no improvement in spite of all treatment and she complained not only of pain in the wrist and hand but of nervousness and insomnia.

Fig. 224.—Anteroposterior view of hands showing apparent decalcification of the lower ends of the right ulnar and radius as compared with the normal bones of the left upper extremity (November 20, 1928.)

Fig. 225.—Same as Fig. 224, lateral view (November 20, 1928).

Her previous diseases appear interesting from their possible bearing on her nervous system. She had measles and whooping-cough complicated by pneumonia at six, pneumonia again at eight, and scarlet fever at ten. At thirteen she complained of back pain but no pathology was revealed. At this time she had a menorrhagia but after four months appeared well. Menstruation began at twelve and has always been irregular. The periods last five days and come every three weeks, occasionally every ten days, and occasionally every thirty days. Three months ago the menstruation lasted two weeks. There has never been any pelvic pain. The sensitiveness to pain is evident.

Physical examination revealed a perfectly normal girl of sixteen with the exception of a swollen right upper extremity. She had large eyes, placid face, rather extremely sensitive nature, easily moved to tears and smiles. The complexion was smooth and clear, eyes blue, hair blonde, and she impressed one as being emotionally unstable and of a decidedly neuropathic constitu-

Fig. 226.—Same as Fig. 224, except taken on December 20, 1928.

tion. She had complained so much about the pain in the arm that the forearm and hand had been bandaged and supported by a splint. She could move the fingers only slightly because of the tenseness of the skin and the marked edema. It was a spade-like hand, the greatest edema being over the dorsum, and pitting was easy. It had the same appearance as a foot with the huge edema of congestive heart-failure.

Laboratory examinations were negative throughout, including urine, blood, gastric contents, stool, and basal metabolism. The teeth and sinuses were normal, though the *x*-ray showed the lower ends of the radius and ulna, the metacarpals and the ends of all the phalanges of the right upper extremity to possess a decided translucency, apparently a definite decrease in their calcium content. The lateral view showed this more definitely than the anteroposterior plate. The hip girdle and bones of the lower extremities were normal.

Upon further investigation it was learned that the patient lived with her grandmother who made much over her. In June, 1927, at the age of fifteen, she had a love affair with a boy in her home town. Her grandmother forbade her going with this boy or his friends. She saw him, however, at school and at other times, but there was always a scene when the subject was discussed at home. Five months after this emotional strain the swelling began. With these scenes were attacks of hysteria and her sentimental and sensitive nature became more apparent. With this emotional experience there was continued grief over the death of her father and she was often found crying in some hidden place.

When the hand was held down for ten minutes it was cold, pied with pink spots to the elbow with the hand and fingers swollen. On measurement the lower extremities were equal and the arms were as follows:

| | Right. | Left. |
|---|---|---|
| Arm, upper third | 28 cm. | 28 cm. |
| Arm, middle third | 26 " | 25.5 " |
| Upper, lower third | 24 " | 23 " |
| Forearm: | | |
| Upper third | 24 " | 23 " |
| Middle third | 21 " | 21 " |
| Lower third | 18 " | 15.5 " |
| Hand | 22 " | 18 " |

Much psychotherapy was used and encouragement. The hand was removed from the splint and the dorsum punctured in two places to permit the edemic fluid to drain. This drainage reduced the hand to one-third its former size. The fluid that drained was the fluid of simple edema, a pure transudate. After the puncture and drainage the hand was placed in hot water at a temperature of 98° F. for ten minutes followed by the same time in cold water, three times daily. There was a difference of 1 cm. in the circumference of the hand between the hot water and cold water exposures. The patient was encouraged to use the right hand, which she had to learn to do again, and persuasive psychotherapy and suggestion were used constantly. The small bulb used in the blood-pressure apparatus was given her to squeeze thirty times daily (ten times thrice daily). Blood calcium on December 16th gave a reading of 10.1 mg. per 100 c.c. of blood, well within normal limits. Massage, reading, play, walks, and the usual treatments for a neurosis were used as well as the local treatments for the hand.

Once the subject of localized edema and dropsy is sharply separated in the mind from the edema and dropsy of cardiac and renal origin, there develops the consideration of four very interesting and baffling groups. Such a classification as the following seems at least practical:

1. Angioneurotic edema.

2. Milroy's hereditary edema, which apparently does not appear above Poupart's ligament.

3. Constant edema with periodic exacerbations, of neuropathic origin.

4. Intermittent articular dropsy, which is not to be confused with Charcot's joint of locomotor ataxia. It may come on periodically and the skin over the joint is neither hot nor red. It seems a part of a general neurosis.

However, such cases do not occur except relatively rarely and no one clinician has had very much experience with the group as a whole. Cases of angioneurotic edema and Milroy's hereditary edema are easy of diagnosis and capable of classification. Cases that fall into divisions three and four are more susceptible to difference of opinion.

While in the beginning the complaint in this patient seemed to have begun over in the right wrist there was no evidence that there was any arthritis in this joint, and for months the mass of the edema was in the tissues about the metacarpal bones and the hyperesthesia in the skin and tips of the fingers of the right hand.

This case seems to belong to the third group of neuropathic edema with exacerbations and having a neuropathic origin. Neuropathic dropsy is more expressive of the condition than is neuropathic edema because the pitting was extreme and the drainage excessive. The edema gradually decreased. The middle and upper third of the forearm and the lower one-third of the arm did not pit. It is said that the children of an alcoholic parent tend more to angioneurotic edema. The father of this patient was apparently suffering with dipsomania and died of acute alcoholism. Mueller, of the Mayo Clinic, presented in November, 1928, a case of angioneurotic edema appearing in a seven-day cycle. Oppenheim, on page 1325 of his text-book of "Nervous Diseases," calls attention to the periodic occurrence of articular dropsy. Sydenham talked of edema in hysteria and Charcot tried to lay the foundation for a Charcot type of angioneurotic edema. Angioneurotic edema recurring at definite intervals and intermittent articular dropsy do occur. "Blue edema" is the

name given a "hard, elastic swelling with a decrease in the temperature of the skin." The hard edema after traumatism is well known as illustrated by a blow on the skull. White edema is simply "blue edema" in which the skin is pale and bloodless, but hard without pitting, the so-called "oedeme blanc."

Whether in this case there was any relation between the neuropathic constitution and hysterical temperament of the patient and her edema or a more particular relation between the domestic scenes and her unfortunate unimportant love affairs that preceded the edema, are questions more of opinion than of fact. What caused the decalcification of the bones of the forearm and hands is another interesting matter. She was an extremely interesting and attractive young girl in a very unfortunate domestic environment of petting and senility. Whether had she been at boarding-school under normal surroundings this edema would have occurred is another interesting hypothesis. She had the physical appearance and the conversational power of a girl of twenty rather than a girl of sixteen. Whether the decalcification was the result of the same cause that produced the edema or from disuse, is a difficult question. But most important of all is that chronic neuropathic edemas are curable, first, by puncture and drainage; second, by constant use and activity of the limb involved; third by a general upbuilding treatment; fourth, psychotherapy and a normal environment are at least useful aids.

## ACUTE PELLAGRA ASSOCIATED WITH A MANIC-DEPRESSIVE PSYCHOSIS DEVELOPING AFTER A FIVE-YEAR PRE-PELLAGROUS PERIOD

MRS. W. L. B., aged thirty-eight years, married, living in Florida, came on February 2, 1928 complaining of nervousness. She had been married thirteen years and had one miscarriage in 1920. The family and marital history was otherwise unimportant. Menses came for three days every three weeks and for the last year had been painful. She had a mild attack of influenza in 1918 and another in 1923. After the last attack and for three years thereafter she felt below par, neither very sick nor very well. She gradually grew more and more nervous, introspective and became constipated. During this time she consulted several physicians and two years ago, on account of persistent indican in the urine, was put on a nearly protein free diet, on which she had lived during the whole of 1926 and 1927. Her condition had grown gradually but constantly worse. The diet for the two-year period had averaged, for breakfast, raw or stewed fruit, grits, butter, one egg, and rarely a piece of toast. For dinner, two vegetables, rice once in two weeks, meat or chicken once weekly, one corn meal or bran muffin. Vegetables were limited to cabbage, carrots, turnip greens, asparagus, English peas, and okra. For supper she had hot chocolate and toast with only occasionally oatmeal, during the winter months. In the summer she made her supper of a salad, bread, lemonade, or chocolate milk.

The patient is an educated woman, the wife of a lawyer and she formerly helped him in his practice. For the past two years, however, this had been impossible though she had tried to do church work, civic and club work but her exhaustion had finally necessitated omitting these very pleasant duties, and for eight months she had been in bed most of the time. For four years there had been some cystitis with recurring and mild acute attacks and some transient burning and pain on urination. Some of her frequent urination she attributed to her nervousness. She voids on an average of six times a day and once to six times at night. She thinks the cystitis came about four years ago, though from childhood urination had been more frequent than normal. She had always had a normal yearning for motherhood and she has been somewhat depressed at her inability to become pregnant since the miscarriage of 1920. Eight months ago her nerves collapsed and her condition has steadily grown worse until the depression is exaggerated, the periods are more frequent and longer, and her personality is radically changed from the bright woman of former years. She desires so much to help her husband as formerly. She feels that she fritters her time away in ill health, despondency, and tears. Two months ago she began to talk to her husband of the long sleep when at last she could rest. Her physician had so impressed upon her the importance of indican in the urine that she had tested it daily and kept

a bottle of chloroform for this purpose. She had made up her mind to commit suicide both by internal use and saturation of a handkerchief to produce anesthesia.

Many physicians had been consulted over this five-year period. Each had made a diagnosis of cystitis because of the continued pus in the urine. And various other contradictory diagnoses were made. One doctor had

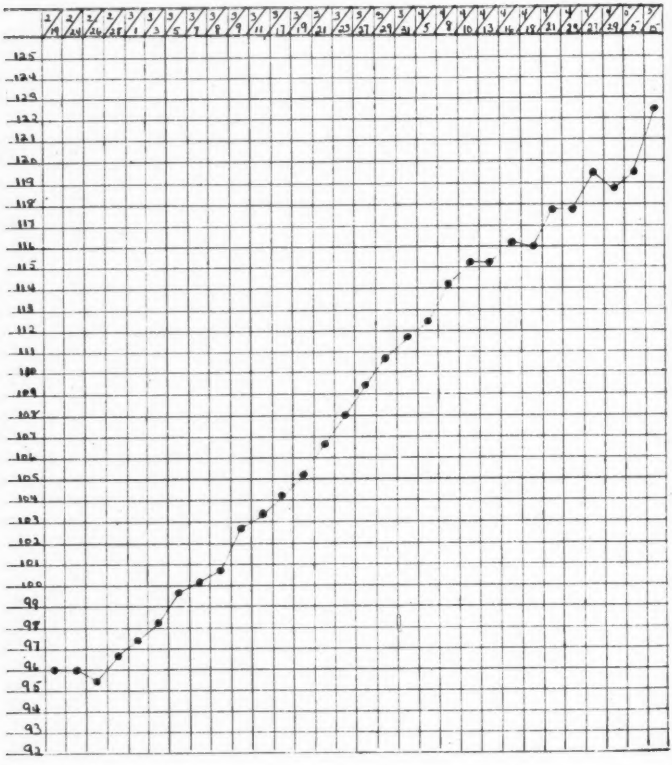

Fig. 227.—Note weight on entrance, Feb. 2, 1928 (96 pounds) and (122 pounds) on dismissal May 5, 1928.

advised a pan-hysterectomy and another advised against it. One doctor had advised the removal of all the teeth and another had seen no reason for the removal of any of the teeth.

Some strange things had happened to her in the course of the last five years. She was formerly never troubled with gas or indigestion and now gas

and indigestion are frequent, gas more when she has extreme nervousness. She was always constipated but in the last month has developed diarrhea and the diarrhea, weakness, and nervousness seem to increase together. On the train the night before coming to the office she had six stools, yellow in color, apparently containing neither blood nor pus and there was no griping nor other abdominal disturbance. For three months her hands and feet had been dry and burning.

The patient was a thin, sallow woman, 5 feet, 3 inches tall, and weighing 96 pounds though her normal weight is 120. She had lost 20 pounds in eight months and estimated her strength to be only 40 per cent. of the normal. Her lips were a bluish-pink, lower lip slightly swollen and everted, both lips dry and an excoriated, reddish area was in the angle of the mouth—the so-called rhagades. The pharynx was inflamed as was the oral mucosa. The tongue was beefy red, particularly on the margins and tips, and underneath the anterior one third. There was an active simple glossitis and the gums were red, swollen, and glistening. The thorax was negative. Blood-pressure 110/70 mm., pulse 96, temperature 98.6° F. The abdomen was negative except for slight tenderness on palpation in the right lower quadrant. A cedar-wood, bilateral eruption occupied the dorsum of each hand. It extended upward, involving and encircling the wrist. The skin over the fingers was dry and scaly and the folds over the knuckles seemed increased. The thenar and hypothenar eminences of the palm of the hand were distinctly flattened and the thumb rotated more like the thumb of an ape than the thumb of man. The fingers were cold and on separation and extension a definite somatic tremor was present. The elbows were rough and branny.

While taking her history she burst into tears continually, talked about her nervousness and moaned over her irritability and her lack of mental and emotional control, her necessity for suicide, her inability to help her husband, her feeling of the certain end, of the on-coming long sleep, of the inability of anyone to help her, of her husband's helplessness and of her mistreatment of him on account of her illness. During examination this moaning and groaning, pathetic creature could but arouse sympathy particularly when one contrasted her present condition with the erect, brilliant, cultured woman of past years.

The neurologic examination was negative except that all the deep reflexes were increased. Pelvic examination showed a definite vaginitis with leukorrhea which she stated had developed during the past four weeks. Laboratory examinations showed normal urine, except for one plus pus; normal stool, negative Wassermann, and blood with a hemoglobin of 60 per cent., erythrocytes 3,230,000, color index 0.9, leukocytes 6350, and the differential of 18 lymphocytes, 2 large mononuclears, 1 transitional, 78 neutrophils, and 1 eosinophil. The diagnosis was immediately plain because only one disease is characterized by such a gradual insinuation, an unbalanced diet over a long period, a gradual loss of weight, the development of great nervousness and a definite psychosis, a bilateral symmetrical eruption on the hands and encircling the wrist, branny elbows, red and sore tongue, mouth, and throat, a recent vaginitis, a constipation that had reversed to a diarrhea, burning hands and feet, gas, anorexia and indigestion, insomnia, emotional insta-

bility and a gradual but definitely apparent deterioration of the mind, all associated with an exaggeration of the deeper reflexes.

She was put in the hospital on the same date of her arrival at the clinic, February 18th, and four days later, February 22d, she was disoriented both in time, place, and person, and was convinced she was doomed to die. Fortunately she could and did eat and she was given a 2500 calorie, high protein diet with emphasis on meats, milk, eggs, peas, and beans. Brewer's yeast in 2-dram doses was given after meals, sedatives forbidden, and dilute hydrochloric acid and tincture of nux vomica given in 1½ c.c. doses after meals. Her window was kept open constantly in the coldest winter weather, water and milk served ice cold, she was permitted to keep her hands and burning feet exposed to the cold air, the heat was turned off in her room and she was given a tepid tub bath at ten in the morning and four in the afternoon, daily. Ten days later, February 28th, the hydrochloric acid was increased to 2 c.c., an occasional dose of castor oil was given on waking in the morning. On account of her psychosis two nurses were necessary from February 18th to March 2d, but on March 9th both special nurses were discharged, so marked was the improvement. There were lapses into disorientation but finally the patient was controlled mentally by the advice that "for the present everything she thought was wrong, and her duty to herself and to her husband was simply to eat what was brought her, and that time would bring about complete recovery." March 12th progress note of the hospital record testates: "A gradual improvement is continually noted. Complains of hands and feet. Says they feel tired, hands feel puffy and they burn. She knows now, since her improvement, how weak she is." Between March 2d and March 20th there were several attacks of acute labyrinthitis, a sea-wave bed, a typical Ménière's syndrome. She describes these attacks as if the bed is going to roll out from under her and most of the sensations passed from right to left. The burning sensation in hands and feet diminished gradually. Between February 18th and March 19th she had gained 9 pounds and weighed 105 pounds. On March 31st, a slight redness remained under the anterior third of the tongue but the mouth and hands were well. The feet "fired up" on the night of March 29th. Her weight was 111½ pounds. The diarrhea disappeared after the first ten days in the hospital. She was discharged from the hospital with a weight of 122½ pounds, or a total gain of 26½ pounds. During all this time there were occasional attacks of nervousness and of vague and transient pains. A few flurries of diarrhea occurred but she felt better by remaining in bed and eating freely. There was no fever at any time, the temperature usually ranging from 97° to 98° F., the pulse from 80 to 100 and as she improved and gained in weight she began to sleep normally, her temperature gradually rose to normal, pulse dropped to 80 and respiration to a level of 20. Her emotions gradually grew stable, her outlook cheerful and her mind normal. She was sent to the mountains of North Georgia for six months with the following directions (May 15, 1928):

1. For the next year be as happy, as natural, and as vacant minded as possible.
2. Avoid any social, outside, civil, or ecclesiastical duties, except purely as a matter of pleasure, and without strain.

3. Get up in the morning half hour to an hour later than usual. Lie down after dinner two hours, and to bed at 9 P. M.
4. On Wednesdays and Sundays remain in bed until noon, except may be up for breakfast.
5. Learn to bathe in cold water.
6. Always drink cold water.
7. Learn to keep the window up day and night and to get chilled once or twice daily.
8. In the warm summer days, a morning and afternoon cold bath or sponge bath would be well.
9. No hurry. No worry. No firing. Don't fire up—sit down.
10. During meals take 20 drops of the tincture of nux vomica and 20 drops of the acid, in water, through tube.
11. Teaspoonful of Brewer's yeast in glass milk once daily.
12. Lime-water for milk.
13. Diet: *Breakfast:* Two eggs, bacon or meat, fish or fowl; fruit, cereal, as oatmeal or cream of wheat; glass milk.
    10.30: Glass whole milk or butter milk.
    *Dinner:* Vegetables, meat, fish, or fowl. One hard-boiled egg, beans, peas, butter, gravy, cheese, fruit salads, fruits raw or stewed. Glass milk.
    4.00 P. M.: Glass whole milk or butter milk.
    *Supper:* Choice from foods listed for breakfast and dinner. But be sure to eat meat, fish, or fowl, and drink a glass of milk.
    *Bedtime:* Glass milk.
14. Maintain your weight between 120 and 130 pounds.
15. Do not allow idealism, emotions, education, or mental preoccupation to interiere with bathing, rest, quiet, and overeating as compared to your former diet.

A letter from her illustrates very definitely the mental and emotional state of these patients, the persistent optimism that is necessary, the psychotherapy that must be used, and the results that are obtainable with the general outline of treatment as above indicated.

'July 5, 1928.

"I fear you and Dr. Bonner have decided that I am like many others who go away and fail to let you hear from them. And I promised her I'd be different. Well, really, I have written you several letters but upon rereading them would not send them, because they were too optimistic or too blue, colored by my feelings at the time of writing.

"My condition, taken as a whole, has been very satisfactory—having had few of the old bad symptoms; some good days and some bad ones, but always with the sunshine of hope ahead and a slow, steady gain in weight, until last week I lost a pound, then picked it up again and now weigh a little over 133 pounds. The weather up to that time had been very kind to me; either cool or rainy. But for the last two days we find the thermometer standing at 89 at noon—I then resort to frequent cold sponges.

"However, I found myself slipping before this hot spell set in. My stomach and bowels pain, with much gas in intestines, side and around heart; with throat and mouth sore; the bowels looser, one day four stools of pale yellow, spongy consistency, at which I left off yeast; frequency now diminished but texture the same, headache, shifting from front to rear of head; old feeling of swelling under left eye and right foot, at times over whole body; occasional little pimples on various parts of body; constant blisters and itching on toes; occasional bright spots in cheek, especially left side; some firing of limbs up to knees. The complexion, which has been clear is darker and cloudy looking with dark circles under eyes. And I do not sleep well at nights.

"When I was unable for several days to throw these troubles off, I got discouraged, and I am ashamed to confess, wrote you a blue letter and had a good cry. I did not let the folks here know it however, and now have myself in hand again and have torn up the letter. For I have been in fine spirits with good control and poise, and with judgment clear and reasonable. When Mr. —— was here two weeks ago, he was delighted with condition and appearance.

"I have tried to follow instructions and have had fine co-operation and supervision on the part of father and mother and have succeeded admirably, except perhaps as to the injunction to "be vacant-minded." I can't do it. But I have surprised myself by the ease with which I am dismissing troublesome matters. Hope I'm not getting too selfish.

"Now, in describing these symptoms, I do not mean that they have returned with the same intensity as when I first went to the hospital but they are distressingly uncomfortable and have lasted longer than at any previous time since I began to get better.

"Do you think that vinegar or beets, or acid of fresh tomatoes, or any other special article of food would be apt to have bad effects? I have tried to study reasons for these recurrences but have reached no satisfactory conclusions.

"Have had one rather restricted menstrual period, accompanied by quite a bit of pain, but not as much as the former period which was the worst I had ever experienced. Another is about due but thought perhaps these cold sponges are delaying it. Would that have any bearing on all these other disturbances?

"Do you suggest that I increase the amount of exercising to try to control my weight. I find that I feel better on moderate amount of stirring around. I tried dusting and would fire up each time. I walk some but not a great deal."

Our reply was as follows:

"Thank you for your letter of July 5th. We had been expecting to hear from you.

"1. You are doing well. You must do a good bit of overlooking—more overlooking than you have been doing. Remember that you are an educated woman, tuned and timed to distinction and differences. You must cut the telephone wires between your body and your consciousness.

"2. Don't expect too much too fast. One never realizes how sick he was. You were very sick. We are in the summer and you are doing well.

"3. One great mass proof and symptom that you are getting well is that you are holding your weight. A pound or two more or less makes no more difference than a point or two in the stock market.

"4. Be not only of good cheer but of good courage. Think of Robert E. Lee's having to surrender in a dress suit.

"5. Your mind is too active. Give the nervous system time to renew itself. Begin to walk a little outdoors daily, particularly in the cool of the afternoon or after supper. Get a little physically tired and stretch your limbs. Take more exercise but don't overdo.

"6. Leave the menstrual period to nature."

In conclusion:

(1) It is very evident that for the five years preceding the outbreak of acute pellagra in January, 1928, this patient was pellagrous. She then had acute pellagra.

(2) Deficiency disease, as illustrated by pellagra, is usually preceded by longer or shorter periods during which the patient is suffering from the deficiency and the deficiency becomes cumulative like a preferred stock, but differs from the preferred stock in declaring the unhealthy dividend of a pellagra.

(3) As Berry has so clearly stated, the brain is the physical basis of the mind, no brain, no mind. And in pellagra a diseased brain with degenerative changes in the cells means a diseased mind which we call the psychosis of a pellagra.

(4) When the deficiency is succeeded by a balanced diet with accent on proteins and vitamins, the disease pellagra disappears, the physical improvement is marked, the psychosis fades, and the normal mind reappears and emotional instability is succeeded by the ordinary behavior of a normal psychology.

(5) This patient was more educated than ignorant; more intellectual than physical. In the midst of plenty she had eaten an unbalanced diet, and in the name of science and because indican was magnified had for two years lived on a nearly protein free diet. A wrong belief, even in medicine, brings its own terrible results.

## SCLERODERMA ASSOCIATED WITH SYMPTOMS OF ERYTHROMELALGIA AND MYXEDEMA

F. G. W., aged sixty years, a native of England though a resident of Georgia for many years, a commercial secretary by occupation. Height 5 feet, 3 inches, normal weight 165 pounds with present weight of 126 pounds. He had lost 39 pounds during the year.

He was seen August 2, 1928 complaining of "trouble with the circulation" and "inability to use the hands normally," which had lasted for eighteen months. The family and personal history is unimportant except that he had typhoid fever at the age of eighteen and a mild sickness, diagnosed acidosis, just before the present complaints began. The habits were good though he drank two cups of coffee, smoked five cigars a day, used sodium chlorid excessively, soda bicarbonate freely, and delighted in rich foods and large meals.

The general appearance of the patient was that of a weak old man, a little stooped, with glaring eyes, a discoloration of the skin, and an uncertain gait even with a cane and then more waddling than walking and very wobbly on turning. The head was held slightly forward, the chin dropped, and the features were rigid. The lips were set and the mouth opened and closed stiffly. The skin of the forehead was moist and oily. The eyes were bright blue, had a fixed stare and the lids closed rarely. There was a one plus arcus senilis and pin-point pupils that did not react either to light or accommodation. Ophthalmoscopic examination showed a first degree arteriosclerosis. The face was a reddish brown color resembling the appearance of a boy who had lived at the seashore for a month. There was a set expression, and the skin was smooth. The hands and arms had the same pinkish-purple color; the skin itself thickened to the midarm with a leathery feel. The nails were swollen whereas the hand itself showed distinct atrophy of the muscles. There was marked tremor of the fingers and the skin was tight and fingers semiflexed and could not be fully extended. The nails were cyanotic, ridged, and brittle. They would break easily. The hands and arms were held stiffly like a soldier on parade. The fingers seemed larger than normal in contrast with the bony hand. There was limitation of movement increasing from elbow to wrist to fingers. The skin of the fingers was tight, clung closely to the bone, and could not be pinched up. He had noticed from the beginning that they felt like wood and with their stiffness, their tightness, the change in color, their coldness, even on a hot day, it was very evident why he complained of poor circulation and stiffness of the hands. Here was typical sclerodactylia with pigmentation. The tendons were tender and stiff. The anterior tibial artery was not palpable, but both posterior tibials pulsated. The skin of the feet and legs resembled that of the hand and forearm. A marble-like induration had taken the place of the normal skin. Inflammation occurred around several of the toe-nails as it did around the finger-nails.

The feet could neither be extended nor flexed completely and were apt to remain in the position in which the examiner placed them. He wore tennis shoes because the weight of ordinary shoes was unbearable. The indurated marble-like skin extended from toes to midthigh, from fingers to midarm, and involved the neck and face.

Fig. 228.—Note the glaring eyes, the fixed expression, and the smooth set face. The pigmentation of the hands and feet is plain. The white nails stand out in contrast. (The dark spots are errors in development.)

Fig. 229.—Note the expression of weakness, emaciation, and the short lips. The excessive pigmentation of the hand and forearm is in marked contrast with the arms and shoulders.

The strength had decreased 75 per cent. The dynamometer reading was only 20—70 to 100 is normal strength. He was very weak and the metabolism test exhausted him. The pulse was fast, 148 after a few steps, and

the blood-pressure 100/60 mm. Basal metabolism test was plus 10 per cent. The Goetch test with adrenalin showed a normal reaction though at the time of sweating, forty-five minutes after the adrenalin was given, the blood-pressure was 90/60, with pulse 102. The tonsils were two plus infected. Teeth normal. The body was emaciated. The thyroid gland not palpable. The chest was normal but for a two plus emphysema. The abdomen normal and the abdominal wall flaccid. The anus was relaxed; prostate firm and rounded and painless, one plus hypertrophy. There were soft feces in the rectum.

Twelve-hour urine, 625 c.c., a specific gravity of 1.012; acid; a trace of albumin; a few red blood-corpuscles, and pus-cells. The hemoglobin was

Fig. 230.—Pigmentation of the face, neck, forearm, and hands is more clearly brought out in this picture, and the contrast between the tight skin of the fingers and their semiflexed position with the bony knuckles is also evident.

85 per cent.; red blood-cells 4,600,000; color index 0.92 per cent.; leukocytes 15,150; lymphocytes 5, neutrophils 83, eosinophils 1, neutrophilic myelocytes 11. Malarial parasites were not found. The Wassermann and Van den Bergh tests were negative. Complete series of *x*-rays of bones, organs and extremities, including the skull, showed no abnormalities except for a first degree arthritis of the dorsal vertebræ and a spastic colon from the mid-transverse to the sigmoid.

Neurologic examination showed hyperesthesia of the soles of both feet. No disturbance in touch, pain, or temperature over entire body nor of organic sensations. All movements were slow, apparently from muscular weakness chiefly and stiffness of the skin. Cranial nerves normal. When the seventh

nerve was tested he could whistle, smile, and puff his cheeks normally. Finger to finger test and finger to nose test normal. Reflexes of upper extremities normal. Finger tips painful at times. Abdominal reflexes present. In the lower extremities there was pain on pressure over the gastrocnemius muscles. The patella and Achilles's reflexes were present. The sense of position of the joints normal. Babinski, ankle clonus, and Romberg negative. Sitting on the edge of the bed with arms hanging down they became pinkish-purple to above the elbows and the legs to just above the knee. The toe-nails became white and gradually there was slight swelling of hands and feet. Bladder and rectal control normal.

September 11, 1928 he consulted a physician in Baltimore who confirmed the diagnosis of scleroderma and noted that the disease had extended to an involvement of practically the entire body the more extensive changes were in the extremities. At that time the hemoglobin had dropped to 71 per cent. and the white and differential count were normal as was the blood-chemistry, stool, urine, and phthalein excretion. The gastric analysis showed a free acid of 5 per cent. and a total acid of 24 per cent. Sugar tolerance test showed fasting 0.09 per cent., half hour 0.133 per cent; one hour 0.144 per cent.; two hours 0.140 per cent.; three hours 0.103 per cent.; which would indicate some difficulty in normal glucose metabolism.

A blood-sugar was done March 28, 1928 and found to be 0.11 of 1 per cent. and chlorids 550. In April, 1928 he presented the typical picture of erythromelalgia except for an absence of pain. Instead of red and painful feet there were simply the red feet and legs. There was no scleroderma demonstrable at this time. In June, 1928 there was an edema of the feet and legs and hands and marked induration, with subnormal temperature, apathy, and sleepiness so that he would sleep for twelve to fifteen hours at night and repeatedly during the day. A diagnosis of myxedema was made by the attending physician, thyroid extract was administered and there was marked improvement in the induration and edema with decreased sleep and increased mental and physical activity. Treatment was merely palliative. He grew gradually weaker, developed influenza December, 1928, an anuria, had three uremic convulsions with death at 11 P. M. the same day. There was no autopsy.

Osler in his article on "Diffuse Scleroderma" in his Modern Medicine discusses the great difficulty of diagnosis in the early stages. The disease may begin with an edema with very slight erythema or as in this case, with very marked erythema and very slight edema. It has been mistaken, as Osler stated, for an early leprosy. April 2, 1928 two opinions were expressed, (*a*) one that it was a typical erythromelalgia and (*b*) another that it was a case of circulatory asthenia. In June there was much evidence that it was a case of myxedema though no metabolic reading could be done at that time. August, two months later, the marked

erythema had disappeared, the coppery pigmentation on the extremities had developed, the bronze tint of the face and body, and scleroderma of the face and extremities were evident. By September, a month later, the scleroderma had included the whole body and the erythema had disappeared. Throughout the case the asthenia, the low blood-pressure, and the pigmentation of the extremities were evident. Wooden fingers, weakness, and red feet and legs dominated the picture in the beginning. The blood-sugar throughout appeared to be normal. The basal metabolism was very difficult to obtain because of the weakness of the patient as illustrated by the variable metabolic readings. The respiratory muscles, in common with the other muscles when the case was seen at an advanced stage, were so weak that even normal respiration for a ten minute period was practically impossible. The terminal phalanges were normal.

Kaposi's classification into the three stages of elevation, induration and atrophy was present, but in the beginning, the stage of elevation included more a hyperemia and erythema of the skin than an edema. The fingers were certainly stiff, the hands helpless, and the muscles shriveled and atrophied. There were no ulcers though there were several small boils on the last phalanx of the fingers. The lips and alæ nasi were shortened. It would appear that here was a trophoneurosis, but it would be difficult to determine even a theory as to the cause. He was a man who worked in high gear, overate, and had an abnormal craving for common salt and common soda. Several different diagnoses were made and each seemed within the law of probability at the time. Finally the true disease unfolded. As Stokes has pointed out the pathology is simply an endarteritis of the capillary bed with increase in the connective tissue and is certainly not specific. Endarteritis and fibrosis, with the notable thickness of the skin, are probaby present in every case. A focal infection was present in the tonsils. A mild influenza was too much for the already asthenic body.

Christian records a case that succumbed quickly to a pneumonia after an emphysema. The etiology of sclerosis remains as dim as ever.

CLINIC OF DR. G. CANBY ROBINSON

NASHVILLE, TENN.

## A CASE OF CORONARY OCCLUSION, ASSOCIATED WITH VENTRICULAR PAROXYSMAL TACHYCARDIA

OCCLUSION of the coronary arteries has been recognized by pathologists as a not infrequent cardiac lesion as long as careful autopsies have been performed, but until comparatively recent times the lesion was considered rapidly fatal and was not associated with a definite clinical picture. On this account the diagnosis of coronary occlusion was made during life very rarely and with great caution. During the past twenty years, however, clinicians have learned to associate occlusion of the coronary arteries with very severe, although not necessarily fatal, disturbances of the circulation. The publications of James B. Herrick have been of first importance in acquainting the profession of this country with the clinical manifestations of coronary occlusion. The effects of this lesion have also been studied extensively experimentally by Fred Smith[3] and others, and it has been demonstrated that dogs may survive the ligation of coronary arteries. The effect on the heart of coronary occlusion varies naturally with the size of the artery occluded. At the present time varying degrees of clinical manifestations, from transient chest pain and discomfort closely resembling true but mild angina pectoris to severe, sudden, and often fatal cardiac failure, are recognized as resulting from coronary occlusion. The differentiation of coronary occlusion from angina pectoris may be difficult. As a matter of fact some cases of angina pectoris have a partial occlusion of a coronary artery, which probably accounts for the symptom complex which was observed in the case to be reported. The exact relationship is still unsettled. Angina pectoris is essentially a recurrent set of fairly characteristic

symptoms of short duration, frequently leaving the heart without definite signs of any structural change or evidence of heart-failure. The symptoms arising from coronary occlusion, although often of the same general character as those of angina pectoris, may be very severe and of longer duration, and repeated attacks are not usually precipitated by physical or mental exertion. The symptoms of coronary occlusion are usually accompanied by a moderate increase in the leukocyte count, and a slight elevation of temperature may also occur. The detection of a pericardial friction rub sometimes furnishes evidence that cardiac infarction has occurred, and symptoms of circulatory failure generally follow occlusion of a main branch of a coronary artery. On the other hand with sufficient clinical evidence to justify the diagnosis of coronary occlusion, apparently complete recovery may ensue, although once the diagnosis is made, the patient must be always thereafter considered as having suffered cardiac damage demanding strict limitation of activity.

The importance of limiting activity after coronary occlusion was strikingly demonstrated by a famous violinist who collapsed on the stage during a concert, and who then came under my care. The symptoms were typical of coronary occlusion, with intense epigastric pain and greatly disturbed cardiac action. The patient made a satisfactory recovery, but showed some slight evidences of heart-failure, and great cardiac enlargement. The warning was given that the tour would have to be cancelled, and the giving of concerts abandoned. The advice, however, was not followed and sudden death occurred immediately before the first concert that was attempted, three months after the original coronary occlusion.

A feature of coronary occlusion that has aroused interest, and is of diagnostic importance is the disturbance of the cardiac mechanism that may follow the sudden cutting off of the blood-supply to part of the myocardium. A series of cases were reported by Robinson and Herrmann[2] several years ago in which ventricular tachycardia apparently followed coronary occlusion. The relationship was not proved in all of the 4 cases reported, as an autopsy was performed in only 1 case. This type of disturbed

cardiac mechanism has been observed in animals after ligation of a coronary vessel, by Lewis,[1] Smith,[3] Robinson and Herrmann,[2] and others. Several cases, besides those reported by Herrmann and the writer have appeared in the literature. A new case is added in the report of the following case.

**Case Report.**—The patient, a white carpenter of forty-six, entered the hospital in March, 1926, complaining of shortness of breath.

The present illness began three and one-half weeks before admission, without previous symptoms. To avoid a shower, the patient walked rapidly up a hill. At the top of the hill he had an attack of what he called shortness of breath, which consisted of a tight feeling in his throat lasting for about a minute. Three days later, while tearing the roof from a garage, he had a second attack. In this attack there was intense pain under the upper part of his sternum, radiating toward both clavicles and into his left shoulder. At the same time the inner side of the fingers on his left hand felt numb. This pain was accompanied by a "shutting-off" feeling in his lower throat, so that he felt an intense shortness of breath. An observer said that for three minutes his pulse was not palpable. He was frightened and shaken. The pain lasted for four or five minutes, but he did not recover strength for half an hour. After that exertions of any considerable degree were always followed by an attack of pain and shortness of breath. He never had an attack when lying in bed except once, when one came on about five minutes after he had climbed the stairs to his room. All attacks ceased after a few minutes rest. There was no vomiting. There was no shortness of breath between attacks, no edema, no dizziness, and no hemoptysis.

*Past History.*—The general health before the onset of the present illness was excellent. He had malaria in 1907, and measles, mumps, whooping-cough and chickenpox in childhood. In 1901 he had a slowly healing sore on his penis. He received mercurial treatment at Hot Springs for twenty-two successive months. No skin rash, no sores in mouth and no falling hair were observed. One year before admission to the hospital he had urethritis.

He had no headache, and no cardiorespiratory, gastro-intestinal, or neuromuscular symptoms. In 1904 he weighed 165 pounds. The usual weight was 150 and his weight on admission was 135.

*Personal History.*—He was a native and resident of Tennessee and a skilled carpenter by trade. He worked steadily up to the time of his present illness. He used much tobacco and a moderate amount of alcohol. He was married, but separated from his wife after a few years. His wife had one child and no miscarriages.

*Family History.*—The patient's father was living and well at seventy-three. His mother died of pneumonia at fifty-one. Two sisters died of tuberculosis at about thirty years of age.

*Physical Examination.*—On admission to the hospital his temperature was 98.4° F., the pulse 108, and the respiration 20. The patient was a fairly well-nourished man, weighing 135 pounds. He was in no acute distress.

His skin was clear. The pupils reacted well to both light and accommodation. There were no cranial nerve abnormalities and no roughness of long bones. The teeth were good. The trachea was in the midline and there was no tracheal tugging. The chest moved fairly well (vital capacity 3200 c.c.). Slight dullness was found at the right apex but otherwise the lungs were clear. The heart measured by percussion 4.5 by 10 cm., with retrosternal dullness of 7.5 cm. The maximum impulse was in the fifth space and definitely thrusting. The aortic second sound had a liquid musical quality. A systolic murmur was heard over the aortic area and a diastolic murmur was heard at the aortic area, at the left sternal border, and at the apex. This murmur was soft, rather high pitched, and began with the second sound. The blood-pressure was 120/60, and the pulse collapsing. The neck veins were not distended. His abdomen was soft, the liver barely palpable, and the spleen not felt. There was no general glandular enlargement. The reflexes were symmetrical and normal.

The urine gave a faint sugar reaction on one examination, but contained no albumin or casts.

Blood: Red blood-cells 5,900,000, white blood-cells 10,700 (73 per cent. polymorphonuclears), hemoglobin 94 per cent., Wassermann reaction positive.

The report of the teleroentgenogram was as follows: Greatest diameter of the arch is 7.5 cm. M. L. is 9.5 cm. M. R. is 3.3 cm. Longest diameter of the heart is 15.6 cm. Diameter of the base is 12.2 cm. Greatest diameter of the chest is 27.5 cm.

Two days after admission the patient was seen during one of his attacks of pain. Respirations were 28, pulse 101, blood-pressure 175/60. The patient was slightly pale.

Four days after admission, about thirty minutes after his midday meal, the patient had an attack of pain and dyspnea. He complained of a sense of suffocation more than of pain, and localized this sensation deep in the lower portion of his neck and the upper portion of his mediastinum. There was soreness over the sternum. The face was bathed in cold sweat and the complexion changed to a livid hue. The patient was restless and changed his position constantly. Morphia was given with only slight relief. An hour later the patient was nauseated and vomited, and his earlier symptoms reappeared. Nitroglycerin was given with temporary relief. During the afternoon the symptoms became exaggerated. The pulse became very rapid and poor in quality. He vomited from time to time and complained of pain and a sense of oppression so severe that he actually writhed in his bed. At 6:30 p. m. he began to suffer paroxysmal abdominal pain, associated with involuntary muscular spasm. At 7:45 he was cold, pallid, and slightly cyanotic. The radial pulse was imperceptible. The heart rate as determined at the apex was very rapid, apparently about 160. Twenty minutes later his pulse became extremely irregular for a few moments, but seemed to be stronger. Respirations were shallow and periodic. Shortly before this he became unconscious, having retained his faculties up to that time. At 9 o'clock he was comatose, his head was drawn back, his skin mottled. There was Cheyne-Stokes respiration with apneic periods of about forty-five seconds, during which there were ineffectual gasps. Occasional coarse râles were

heard over the lung bases, but air entered the lungs well. At 9:30 the pupils dilated and the respirations became more shallow. At 9:40 the patient died.

Electrocardiograms were taken on admission (Fig. 231) and again on the day of his death (Fig. 232).

It is seen that a striking change took place in the cardiac mechanism. The records made just before death indicate a cardiac rate of 166 beats per minute.

The clinical diagnosis was syphilis, syphilitic aortitis, dilatation of the arch of the aorta, aortic regurgitation, angina pectoris, and ventricular paroxysmal tachycardia with suspected coronary occlusion.

The anatomical diagnosis made at autopsy (and reported by Dr. E. W. Goodpasture) was syphilitic aortitis, partial occlusion of the orifice of the left coronary artery, myocardial necrosis of the left ventricle, aortic insufficiency, congestion of lungs, stomach, liver, spleen, and kidney, focal hemorrhages in the lungs, chronic prostatitis, cirrhosis of the liver.

The pathologist's description of the heart and aorta was as follows: "The heart weighed 400 grams and was somewhat enlarged. The epicardium contained a moderate amount of fat, and in a few places small, whitish areas of scarring were found. The myocardium was soft. On section the muscle tissue was pale reddish-brown in color. At the apex, the left ventricular wall was rather friable, and there was a small focus in which the tissue appeared to be grayish-red in color and almost necrotic. This focus was about 1.5 cm. in length, was outlined by a faint, indefinite line, and involved the inner two-thirds of the thickness of the wall at the tip end of the left ventricle. The endocardium beneath this focus was smooth and shining. No thrombus was present. The rest of the endocardial lining was not remarkable except for a few small foci of old fibrosis, which were present in the leaflets of the mitral valve and in the region of the aortic ring. The cavities of the heart were not enlarged, and the valve rings with the exception of the aortic, the circumference of which was greater than normal, were not enlarged. The right coronary artery was patent and its orifice was not reduced in size. On dissecting this vessel the lumen appeared to be slightly distended, and except for a small focus 0.5 cm. from the origin of the vessel, where there was a small area of sclerosis, the wall was thin and the intimal surface smooth. No thrombi were found. The orifice of the left coronary artery was practically obliterated by an irregular, annular thickening of the aortic wall, and appeared as a small slit about 0.1 cm. in length. A probe could be passed through the opening and into both branches of the vessel. Except for the constriction at the orifice and a small, yellowish plaque 0.5 cm. beyond, the vessel appeared to be negative. No thrombus was found in either branch of the vessel.

"In the ascending and descending portions of the arch, there were small, spherical dilatations which stood out prominently before the vessel was opened. No large aneurysm was found. On opening the aorta from the aortic valve to the bifurcation the intima was found to be markedly roughened. Throughout the entire length of the vessel this roughening appeared to consist largely of small atheromatous plaques, some of which were yellowish and fatty, but the majority of which were calcified but not ulcerated. In the arch and to a small extent in the thoracic aorta, there were many foci of

longitudinal crinkling and irregular scarring which appeared to involve both the media and adventitia as well as the intima. These lesions were most prominent where the fusiform dilatations were seen, and they were intimately intermingled with the arteriosclerotic lesions. Here the aortic wall was thinner than normal and on section was definitely scarred. In one place in the descending portion of the arch there was a small outpocketing of the wall which measured 0.8 x 0.4 cm. in size, and which was about 0.2 cm. deep. Its edges were wrinkled and irregular."

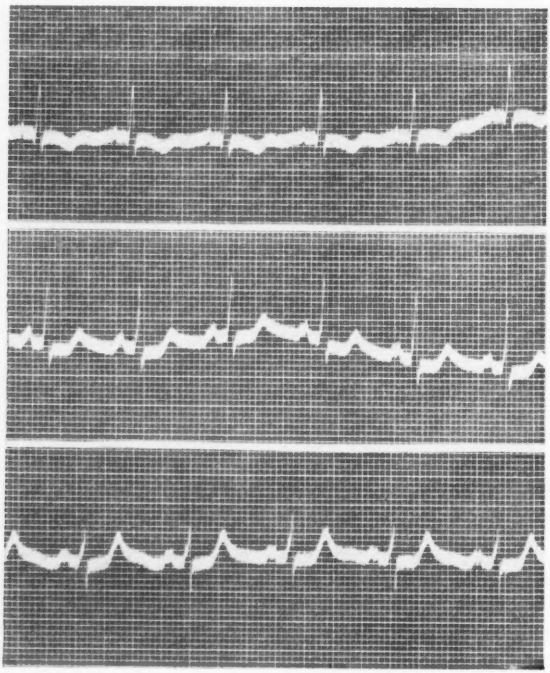

Fig. 231.—Record obtained at time of entrance. Leads I, II, and III. Normal rhythm.

**Comments.**—This case is reported as an example of coronary occlusion which led to myocardial necrosis, and to ventricular paroxysmal tachycardia. It illustrates the disturbed cardiac mechanism, as revealed by electrocardiograms, which may occur with severe damage of the myocardium. Paroxysmal tachycardia arising from an ectopic focus of stimulus formation is graver from

the point of prognosis when the abnormally rapid stimuli arise in the ventricles than when some point in the auricles generates the tachycardia, as is more often the case. On this account it is important to determine the part of the heart from which the rapid stimuli arise. This cannot be done except by means of electrocardiograms, and even then it is quite difficult in some cases to determine with certainty whether paroxysmal tachycardia is of auricular or ventricular origin. The form of the ventricular complexes, the manner of onset and termination of a paroxysm, and the presence of auricular waves not coincident with the ventricular complexes, are all useful in distinguishing the one type of paroxysmal tachycardia from the other.

The records obtained from this patient are shown in Figs.

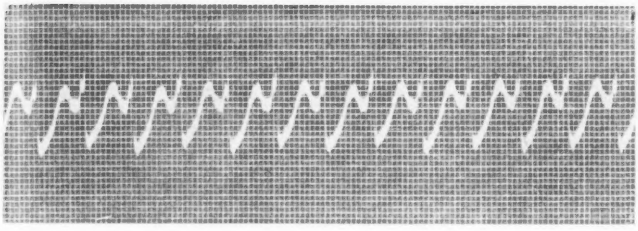

Fig. 232.—Record obtained shortly before death. Lead II. Ventricular tachycardia.

231, 232. Figure 231 shows the record made when the patient entered the hospital. This record shows only minor deformities of the ventricular portion of the curve, changes not by themselves of much significance. Figure 232 illustrates the record made a few hours before the patient's death, after the development of the rapid regular rhythm. No auricular complexes can be identified with certainty. The ventricular complexes show the widening and the shape associated with block of a main bundle-branch or with origin of the impulse in the ventricle itself. They also exhibit a striking alternation in the extent of the excursion. The rate of 166 and the shape of the ventricular complexes indicate that this tachycardia probably originated in the ventricle.

The case that is reported is of interest from the clinical point of view of distinguishing coronary occlusion from true angina pectoris. The history in this case is in keeping with the latter diagnosis, while the physical examination revealed evidence that would lead to the belief that the coronary orifices were probably distorted, narrowed, and partially closed. The case presents a combination of symptoms and lesions that would favor the belief that some cases of angina pectoris are caused by lack of blood-supply to the myocardium due to a lesion of the coronary vessels. Such lesions are, however, lacking in many fatal cases of angina pectoris.

I wish to express my thanks to Dr. C. Sidney Burwell for his collaboration in preparing this report.

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CLINIC OF DR. V. P. SYDENSTRICKER

AUGUSTA, GA.

## WILSON'S DISEASE (PROGRESSIVE LENTICULAR DEGENERATION)

THIS seventeen-year-old white boy who is presented for your consideration manifests all the essential features of one of the rarer neurologic syndromes, one which was first described definitely by S. A. K. Wilson, in 1912, and called by him "Progressive Lenticular Degeneration."

The patient, Charles H., was admitted to the hospital on April 16th of this year (1923) complaining of disturbance of speech, clumsiness of the fingers, and stiffness of the legs with difficulty in walking. His past history is singularly devoid of interest. He had influenza during the pandemic of 1918 and dengue fever in November, 1922. Careful questioning failed to reveal any other illness. The family history is likewise negative. The father is living and in good health. The mother died of influenza in 1918. There are three sisters and four brothers all in good health; no siblings have died.

The present illness began three months before admission. At that time his father noticed that the patient tended to hold his mouth open with his face set in a peculiar expression described as "a silly grin"; at the same time he had some difficulty in using his left hand and at times the left arm would become "drawn," the arm flexed on the chest, the wrist flexed on the forearm and the fingers flexed at the metacarpophalangeal joints. At first this grimace and contracture of the arm were transient, but for two weeks before coming to the hospital they were constant. Shortly after the onset the boy began to limp, this limp was due to the left knee being held flexed while the foot was extended on the ankle so that he walked on his toes. About three weeks before admission a speech defect was noticed; the patient slurred his words and mumbled so that he was understood with difficulty. This dysarthria lasted for three or four days, then disappeared for two weeks, to recur on the day before we first saw him. During the two months prior to entrance to the hospital the set, grinning facial expression became more marked, the flexor spasm of the extremities increased and involved the right arm and leg, the boy became very quiet, seldom speaking, although in no sense drowsy or stupid. He had increased difficulty in dressing himself and in working, due to the clumsiness of his fingers and the stiffness of his arms. He had

several severe attacks of epistaxis and on two occasions there was oozing of blood from the gums. For four days before admission the left foot and leg were swollen. There was no pain and no disturbance of sensation at any time. The boy worked at a lathe in a machine shop until the day before he came to the hospital.

Physical examination showed a boy of good bony and muscular development, but of distinctly abnormal conformation. The temperature was normal, the pulse 88 per minute, the respirations 20 per minute, and the blood-pressure 120/75. The facial expression was peculiar, the mouth held open and the lips and face drawn in a fixed inane grin. Speech was hesitant with slurring and at times mumbling of words; almost every sentence was prefixed by a high-pitched laugh.

The bodily conformation was eunuchoid with some feminine characteristics. The arms and legs were disproportionately long and were rounded and tapering, the fingers in spite of work as a mechanic were slender and delicate. There was complete absence of axillary and pubic hair. The mammæ were of feminine type, the nipples large with a wide areola and with glandular and fatty development comparable to that of an eleven-year-old girl. The pelvis was wide, the mons large, the genitalia minute, the thighs and buttocks typically feminine.

The head was anatomically normal, the ears and sinuses showed nothing of significance. The eyes looked normal, extra-ocular movements were well performed, there was no nystagmus. The pupils were normal in size and contour and reacted to light and distance. The fundi showed no abnormalities of nerve head, vessels or retinæ. The nose was negative. The teeth were well preserved though there was pyorrhea, the tongue was protruded in the midline without hesitation or tremor. The tonsils were large with no gross infection, there was no salivation and no dysphagia. The neck showed no abnormality.

The thorax aside from the exuberant mammary development was quite negative. The lungs and heart showed nothing noteworthy. The abdomen was smooth and rounded, the left hypochondrium bulged, respiratory movements were good. The edge of the liver was felt one fingerbreadth below the right costal margin, the spleen reached three fingerbreadths below the left costal margin and extended almost to the midline, the edge was thick and rounded, very firm. No signs of free peritoneal fluid were elicited. The genitalia were very small, comparable in size to those of a six-year-old boy; both testes were present in the scrotum.

The arms were flexed at the elbows and held crossed on the thorax, the hands were flexed on the wrists and the fingers flexed on the hands but the fingers themselves were held in extension and slightly separated. This flexion spasm could be overcome slowly by the patient and readily by the examiner. There was no tremor, athetosis or fibrillation, the muscles were not atrophied; the grip was excellent and the strength of the arms surprising. There was no definite inco-ordination, but movements were performed very slowly. The legs were held flexed as the patient lay in bed with knees drawn up and feet extended on the ankles, movements were well performed and the strength of the legs was good. The boy stood with his knees slightly

flexed and feet extended so that he walked on tip-toe with a curious gait suggestive of festination. After standing for a few minutes the heels could be brought to the floor and station was quite normal. The tendon reflexes were all present and slightly exaggerated. There was no clonus. The Gordon, Oppenheim, and Babinski tests gave normal responses. The corneal, pharyngeal, abdominal, and cremaster reflexes were normal. No sensory disturbances could be detected.

The various routine laboratory examinations of the blood, urine, and stools were negative except for a mild secondary anemia (hemoglobin 65 per cent., red blood-cells 3,842,000, white blood-cells 5350). The phenolsulphonephthalein test showed 60 per cent. excretion in two hours. The blood-sugar was 120 mg. per 100 c.c., the non-protein nitrogen 22 mg. A glucose tolerance test showed normal carbohydrate utilization. The basal metabolic rate was 24 plus. Radiographs of the sella turcica showed no evidence of pituitary abnormality. Fluoroscopic and radiographic examination of the gastro-intestinal tract was negative.

The boy has remained under observation constantly since the 16th of last April with the exception of three weeks in May. His progress during that time has been interesting but depressing to watch. As you see him today (November 24, 1923) he presents many phenomena not present on admission. His general nutrition has suffered, the flexures of the arms and legs have increased, the muscles are more spastic and the spasm is less easily overcome. The coarse tremor of the hands began four months ago, it is increased by voluntary effort and is severe enough to render him quite helpless. His speech is almost unintelligible. He is emotional and weeps if his wants are not attended to immediately. The salivation with resulting dribbling has been present for six months and adds to his discomforts. His abdomen has become distended with fluid and the feet and ankles are chronically edematous; walking is impossible without support on account of the progressive spasticity of the muscles of the legs and feet. Aided he walks with short swinging steps, on tip-toe and will fall forward unless firmly held. During the past month he has developed very troublesome dysphagia. Fever has been present almost constantly, not regular as to degree or time but during each twenty-four hours there has been an elevation of temperature reaching 101° F. on several occasions.

The symptom complex presented by this boy corresponds very closely with the definition given by Wilson[1]: "Progressive lenticular degeneration may be defined as a disease which occurs in young people, which is often familial but not congenital nor hereditary; it is essentially and chiefly a disease of the extrapyramidal motor system, and is characterized by involuntary movements, usually of the nature of tremor, dysarthria, dysphagia, muscular weakness, spasticity, and contractures with progressive emaciation; with these may be associated emotionalism and certain symptoms of a mental nature. It is progressive and after a longer or shorter period, fatal. Pathologically it is characterized predominantly by bilateral degeneration of the lenticular nucleus, and in addition, cirrhosis of the liver is constantly found, the latter morbid condition rarely if ever giving rise to symptoms during the

[1] Wilson, S. A. K.: Brain, xxxiv, 295, 1912.

life of the patient." Here we have a youthful patient who has developed successively spasticity, with curious and characteristic posture of the face, hands, and feet; dysarthria, tremor, dysphagia, emotionalism, and emaciation. There is no true paralysis; no real contracture, the reflexes remain qualitatively normal. In addition to these neurologic findings we have a history of nosebleed and oozing from the gums, there is hepatomegaly, splenomegaly, and recently, ascites, all pointing to hepatic cirrhosis. Our patient presents in addition, evidence of gonadal insufficiency.

The etiologic agent in this disease remains unknown. Wilson found it often a familial disease. No other member of our patient's family as yet presents evidence of the malady. It is the consensus of opinion that the hepatic disease is primary with secondary toxic degeneration of the lenticular nuclei. It is curious that symptoms of cirrhosis of the liver should be so infrequent clinically when profound changes are uniformly present postmortem. Our patient is, so far as I have been able to discover, the first to present definite evidence of hepatic cirrhosis during the course of the syndrome of progressive lenticular degeneration.

*Further Course and Autopsy Report.*—The progress of the disease was rapid. On December 1st slight icterus was noted, the patient lost weight and strength rapidly. Dysphagia became complete so that tube-feeding was resorted to on December 10th. The mental condition became much worse. At night he was delirious; during the day he was drowsy and could be roused only with difficulty. He became incontinent, or was unable to indicate when the necessity for voiding and defecation arose. The ascites and edema increased steadily and the daily elevation of temperature reached 101° F.; a severe secondary anemia developed. On December 28th small decubitus ulcers appeared over the ischial tuberosities; these rapidly increased in size. On January 20, 1924 the temperature rose to 102° F., signs of bronchopneumonia were found. The patient died of bronchopneumonia on January 24th. An autopsy was performed by Dr. E. R. Pund.

*Autopsy Findings.*—(Autopsy done ten hours after death.) The body is that of an emaciated white male about eighteen years of age, 177 cm. long, 40 kg. in weight. Good bony but poor muscular development. Postmortem lividity in dependent portions. Two large, deep, sloughing, ulcerated areas over the ischial regions. Rigor absent. No axillary hair present and very few pubic hairs.

Cranial hair rather thin. Eyes deeply sunken in orbital fossæ; pupils equal, regular, half contracted; scleræ slightly yellow. Nose clean. Sordes on lips, teeth, and tongue. Teeth in good state of preservation. Neck long and thin. Thorax, long and narrow. Mammæ are prominent as soft elevated areas just beneath and around the nipples about 5 cm. in diameter, the left slightly larger than the right. Abdomen distended. Extremities show nothing unusual.

Scalp thin and rather dry. Calvarium of the usual thickness. Dura translucent. Sinuses filled with fluid blood. Pia is transparent and free from the dura except along longitudinal sinus. Cerebrum symmetrical. Convolutions appear somewhat flattened and are not as prominent as usual. The brain is diminished in consistence generally, probably postmortem.

The entire lenticular nucleus on the left side is very soft, dirty yellow in color and its markings are indistinct. This area of softening and discoloration is clearly defined from the remaining portion of the brain by the well-preserved internal capsule. On the right, the markings of the lenticular nucleus are indistinct, but the area of softening and discoloration is confined to that part occupied by the putamen.

Cerebellum, pons, and medulla show nothing unusual.

Diaphragm at fourth right intercostal space and fifth left rib.

Pleural cavities: Free and empty. Pleural surface of left lower lobe and the corresponding parietal pleura are cloudy and injected.

Lungs: Left lower lobe and a small part of the lower dorsal part of the left upper lobe are irregularly increased in consistency containing very little air. The cut surface is granular, very moist and deep red in color and on pressure, mucopurulent material exudes from the cut bronchi. Right lung shows nothing noteworthy.

Pericardium: Cavity contains about 150 c.c. of clear straw-colored fluid. Surfaces are smooth and glistening. Small amount of epicardial fat.

Heart: Normal in size. Myocardium is rather flabby, brownish in color and mottled with a few yellowish streaks more marked in the papillary muscles. Valves show nothing unusual. Coronary arteries patent. In the aorta there are a few minute yellowish plaques in the intima near the aortic valve cusps. Intima of aorta stained reddish.

Esophagus: Nothing unusual.

Trachea and Bronchi: Mucosa swollen and injected. Large amount of mucopurulent material present.

Peribronchial lymph-nodes: Dark purplish in color, increased in size on the left. Cut surfaces soft, homogeneous, and bulge slightly.

Peritoneal cavity: Contains about 2500 c.c. of clear straw-colored fluid. Surfaces smooth and glistening. Viscera in usual position.

Liver: Weight 1072 grams. The entire surface is coarsely nodular. The cut surface is divided into spherical islands of yellow liver tissue varying in size from 0.1 to 2 cm. in diameter, which are surrounded by bands of dense pink tissue. The surface elevation corresponds to the islands of liver tissue and the depressions to the bands of denser tissue. Many of the islands are soft and some are semiliquid. No normal liver architecture is discernible.

Gall-bladder: Distended with thick green bile, ducts are patent.

Spleen: Weight 835 grams. Capsule smooth, cut surface dark red in color and yields thin red blood on scraping. The septa are visible, spread apart by pulp. Malpighian bodiés not visible. In the center there is a fairly well defined area, wedge-shaped, the apex at the hilus and the base at the opposite portion of the capsule (base is 7 cm. in diameter). This area is much darker in color than the surrounding tissue. Several smaller areas of similar nature about 1 cm. in diameter are scattered irregularly throughout the spleen.

Adrenals: Combined weight, 17 grams. Nothing unusual.

Kidneys: Combined weight 380 grams; consistence slightly increased. Capsule strips easily leaving a smooth surface. Cut surface reddish in color,

cortex and medulla in proper proportions and well defined, striæ visible, and regular.

Ureters: Nothing unusual.

Bladder: Firmly contracted, contains a small quantity of clear urine.

Genitalia: Penis small. Testicles quite small and firmer than normal. Prostate shows nothing unusual.

Gastro-intestinal tract: Peyer's patches are readily visible as flat, well-defined purplish areas. Mesenteric lymph-nodes are from 1 to 2 cm. in diameter and purplish in color.

Pancreas: Anterior border green stained, consistence diminished. On section the lobules separate more readily than normal.

Anatomic diagnosis: Bronchopneumonia; bilateral lenticular degeneration; cirrhosis of liver; splenomegaly; ascites; emaciation; hyperplasia of breasts; delayed puberty; jaundice.

Microscopic examinations:

Cerebral cortex: Nothing unusual.

Right lenticular nucleus: Region of putamen; marked gliosis and a few areas of degeneration. No ganglion cells seen. Region of the globus; few areas of gliosis and slight degeneration, some pigment present.

Left lenticular nucleus: Region of putamen; extreme gliosis with marked degeneration, small amount of pigment present throughout, no ganglion cells seen. Region of the globus; marked gliosis with areas of degeneration, yellowish pigment scattered throughout, no ganglion cells seen.

Left thalamus: Marked gliosis and much degeneration.

Cerebellum and medulla show nothing unusual.

Pituitary: Much colloid in the intermediate portion. There are focal areas of necrosis in the pars anterior.

Lungs: The bronchi and alveoli contain varying amounts of blood, serum, fibrin, and polymorphonuclear leukocytes.

Heart: The fibers are small; there are a number of large colonies of bacteria.

Liver: The parenchyma is divided into irregular islands by broad bands of dense connective tissue. In some areas this connective tissue is infiltrated with lymphocytes and a few polymorphonuclear leukocytes and the bile-ducts are increased in number. The liver cells are in various stages of necrobiosis. Scattered throughout are colonies of bacteria.

Spleen: Intense congestion. The lymph-nodules are few in number and very small. The pulp is markedly diminished in amount. The endothelium of the sinuses is heavily pigmented. There are large focal areas of necrosis, also occasional colonies of bacteria. In other sections where the congestion is not so intense there is an increase in the amount of connective tissue about the sinuses.

Adrenal: In the reticular zone of the cortex there are numerous large colonies of bacteria with necrosis of much of this area.

Kidney: The capsule is regular. Of the glomeruli there is nothing unusual. The tubular epithelium for the most part is cloudy and swollen. There is marked congestion of all the vessels.

Urinary bladder: Slight lymphocytic infiltration of the mucosa.

Prostate: Fibrosis throughout, very few glands are present.

Testes: General hypoplasia.

Head of pancreas: There is slight increase in the interlobular connective tissue, also there is fat necrosis in the septa and some slight lymphocytic and polymorphonuclear leukocytic infiltration. The islands of Langerhans are in poor state of preservation. The cytoplasm of the cells stains poorly. Many of the epithelial cells of the glands contain brown pigment.

Bone-marrow: Hypoplasia.

## SICKLE-CELL ANEMIA

BLOSSIE GRIFFIN, the negro girl who is the subject of our clinic, was admitted to the surgical dispensary two weeks ago (September 20, 1928), complaining of an ulcer on left ankle which had been present for a year. It was noted that she was very poorly developed and markedly anemic, she was referred to the hospital for study by the medical staff.

Blossie is thirteen years old; though her physical development is that of a ten-year-old child her mentality is good. Her only complaint is the ulcer on her left ankle, but questioning has brought out some significant facts in her history. She is one of eleven children. Her father and mother are well. One brother aged nine is alive and is "sickly." Two brothers died in infancy of "wasting disease." Five sisters survive and are said to be well. Two sisters died in infancy of unknown causes. The patient herself has never been strong. Ever since she can remember she has tired easily, become breathless on moderate exertion and has had frequent attacks of left-sided abdominal pain which had sometimes been associated with nausea and vomiting. She has had occasional pains in the elbows, knees, and ankles; these were never associated with swelling of the joints and lasted only a day or two at a time. She had pneumonia two years ago; there is no history of other infectious diseases. She has never menstruated. The ulcer of which she complains is the most recent of several which she has had during the past five years. Each one persisted for many months before healing. During her stay in the hospital she has had a low irregular fever with a maximum temperature of 100° F., some days have been entirely fever free.

Physical examination shows a pure blooded negro girl, poorly developed and nourished. She is 5 feet tall and weighs 70 pounds. The skin is smooth, but dry and lusterless; there is no eruption and no edema.

The head is normal in contour, hair is abundant but shows marked temporal recession. The lid-slits are equal and of normal width. The palpebral conjunctivæ are pale, the scleral conjunctivæ are distinctly yellow with a greenish tinge. Extra-ocular movements are good, the pupillary reflexes normal. Ophthalmoscopic examination showed retinal pallor, without other significant findings. The nose is normal. The mucous membranes of the mouth are pale. The teeth are excellent, the tongue is pale but clean. The tonsils are large, pale, with gaping crypts, no pus can be expressed.

The neck is long and thin, there is no thyroid enlargement. The cervical lymph-nodes are large and firm. There is striking enlargement also of the axillary, epitrochlear, and inguinal glands.

The thorax is long, symmetrical, and moves freely with respiration. The mammæ are infantile. The lungs show nothing noteworthy. The apex impulse of the heart is seen and felt in the fifth interspace, 9 cm. from the midline; there is no precordial shock or thrill. The area of precordial dulness extends 9.5 cm. to the left and 2 cm. to the right of the midline; there is a

prolonged, soft, blowing, systolic murmur audible at the mitral and pulmonary areas; otherwise the heart sounds are normal. The heart rate varies from 92 to 104 per minute; there is a marked sinus arhythmia. The blood-pressure is 90 systolic, 60 diastolic.

The abdomen is rounded and bulges slightly in the right hypochondrium; it feels soft; there is no tenderness anywhere. The edge of the liver is felt 3 cm. below the right costal margin, firm, smooth, and rounded. The spleen cannot be felt and no area of splenic dulness can be percussed. No masses can be felt and there is no dulness in the flanks. There are a few scattered pubic hairs. The external genitalia are infantile.

The right leg shows a round grayish scar the size of a quarter over the tibia, 2 inches above the malleolus. The left leg presents a shallow, granulating ulcer approximately 1½ inches in diameter over the midportion of the middle third of the tibia, there are two small scars of healed ulcers between this and the ankle.

The blood is most interesting. On admission the hemoglobin was 44 per cent., the red blood-cells 2,468,000, the white blood-cells 11,200. A stained smear showed the characteristic poikilocytes which we call "sickle cells"; elongated fusiform, banana-shaped, and crescentic erythrocytes which stain deeply and uniformly with Wright's stain. These made up 26 per cent. of the total number of red blood-cells. The red-cell picture otherwise was that of a severe secondary anemia, with anisocytosis, ordinary poikilocytosis, marked central pallor of the cells, diffuse and punctate basophilia and occasional normoblasts. A smear stained with brilliant cresyl blue showed 18 per cent. reticulocytes. The leukocyte count was somewhat lower than is usual in this condition. Leukocytosis up to 60,000 without demonstrable infection may occur. A differential count of 500 leukocytes showed 63 per cent. polymorphonuclear neutrophils, 1.6 per cent.; eosinophils, 0.6 per cent.; basophils 7.8 per cent.; large lymphocytes, 23.4 per cent. small lymphocytes, 1.4 per cent. monocytes, 1 per cent. of damaged cells. Four normoblasts were seen while counting. Malarial parasites were not seen. The platelet count was 280,000. A fragility test showed that hemolysis began at a concentration of 0.45 per cent. NaCl, and was complete at 0.24 per cent. The van den Bergh reaction was strongly positive in the indirect phase. The Wassermann was negative. The blood-sugar was 105 mg. per 100 c.c. and the non-protein nitrogen 24 mg. per 100 c.c. In a wet preparation sealed and allowed to stand at room temperature for twelve hours it was found that all the erythrocytes had assumed "sickle" shapes and that many of the leukocytes had phagocyted erythrocytes. Numerous examinations of the blood since admission have showed no material change in the picture.

The urine was amber colored, acid and clear, the specific gravity was 1.012, albumin sugar and bile were absent, urobilin was present in large amounts, a few granular casts were found on microscopic examination. The phenolsulphonephthalein test showed a total two-hour excretion of 48 per cent.

**Discussion.**—This girl presents all the typical findings of a peculiar blood-dyscrasia which is called "sickle-cell anemia."

It is a familial and hereditary hemolytic anemia analogous in many of its manifestations to familial hemolytic icterus, but quite different in the specific poikilocytosis, the changes which occur in the blood *in vitro*, the postmortem findings, and in its apparent limitation to the negro race. Two cases of this disease have been recorded in patients in whom no strain of negro blood could be determined,[1, 2] and one case has been reported in an Arab,[3] but all other instances, numbering now several hundreds, have been in negroes or individuals having negro blood.

The descriptive term "sickle-cell anemia" was first used by Mason[4] and has been retained by most subsequent observers. It has been extended to include the larger group of individuals not necessarily anemic, whose erythrocytes in vitro undergo changes which give them the characteristic sickle shape. We do not know the exact significance of these changes which occur outside the body, but they are intimately connected with the active anemic phase of this dyscrasia. All recorded cases of active sickle cell anemia have occurred in individuals under thirty-five, and the great majority have been children. In every instance save one[3] in which the parents of these patients have been examined the blood of one or both parents has shown the sickling phenomenon. Among the brothers and sisters of patients with active sickle cell anemia, some few have normal blood, some have the active anemia and the remainder show the sickling phenomenon. In the family of our patient both the father and mother show the sickling phenomenon as does one paternal uncle. All the grandparents are dead. Of the four sibs who were examined, the brother aged nine has sickle-cell anemia with a hemoglobin of 35 per cent., a red count of 2,200,000, and 35 per cent. of sickle cells in his blood. A sister aged seven has normal blood, a sister four and one seventeen show the sickling phenomenon. You should understand that when I speak of the sickling phenomenon the blood looks normal in all respects in dried stained preparations but in wet preparations, sealed and allowed to stand for several hours, the erythrocytes assume bizarre sickle shapes.

Icterus is always seen in patients with active anemia and often occurs in those normal seeming individuals whose blood sickles

in vitro whom we call "latent sicklers." It is variable in intensity and the color of the scleræ is greenish rather than a true yellow. General glandular enlargement and enlargement of the liver seem constant in the active phase. The size of the spleen is variable and depends, I think, on the duration of the disease. At one time we were convinced that an abnormally small spleen was always found; it happened that malaria was present in each of our patients who presented splenomegaly up to 1924. Since that time I have seen 5 patients, all quite young, who had marked splenomegaly without malaria. It is probable that enlargement of the spleen is a regular feature of the disease during its earlier course and that fibrosis with great reduction in size of this organ is a result of the condition rather than a factor in its production. All our autopsies in active cases have been on patients with extremely small spleens. In individuals who presented the latent phase, the spleen is normal or enlarged.

The morphologic changes in the blood in the active phase are twofold, those which are characteristic of the disease and those which are common to secondary anemias. The poikilocytes which give the disease its name are seen in no other condition and no similar deformity has been produced experimentally. Sickle cells are found in relatively early stages of development in the bone-marrow, and though 100 per cent. of an "active" patient's cells may become "sickles" in wet preparations, the bizarre forms which result from the sickling of round cells never look exactly like the sickle cells of fresh blood or marrow preparations. The circulating sickle cell has a concentration of color and high degree of refractility that are all its own. In marrow preparations numerous nucleated sickle cells are seen and not infrequently they are found in blood smears. The anisocytosis, basophilia, large number of reticulocytes, and normoblasts and perhaps the increase of leukocytes are manifestations of bone-marrow activity such as are seen in any severe secondary anemia.

The blood-platelets seldom vary beyond normal limits. The fragility of the erythrocytes is not increased. Mason[4] observed that the cell residue in the lower concentrations of salt solutions as complete hemolysis was approached consisted entirely of

sickle cells, we have been able to confirm this repeatedly, so that it would seem that the sickle cells are somewhat more resistant to hypotonic solutions than normal cells. An interesting phenomenon which is often seen in stained smears and which goes on actively in wet preparations, is phagocytosis of erythrocytes, usually by monocytes.

The mechanism of the sickling phenomenon is still obscure. Hahn[5] has shown that saturation of the blood with $CO_2$ will produce it, and that the reaction can be reversed by saturation with $O_2$. We have been able to confirm this observation, with certain reservations. The reaction can be reversed once or twice, then no amount of oxygen will restore any considerable percentage of the cells to their original form. The true sickle cells in the blood of an active case are absolutely unaffected by oxygen. We have found that reduction of the blood *p* H in vitro to 7.3 or 7.25 causes immediate sickling. However, suggestive these observations in their application to the sickling phenomenon they would seem to be of doubtful bearing on the genesis of circulating sickle cells. Some observers hold the theory that sickle-cell anemia is produced in persons who manifest the sickling phenomenon, by infection or intoxication. It is impossible to say that this is never the case, but it seems more probable that patients with sickle cell anemia offer less resistance to infection than normal persons. We have an autopsy on one patient who died of anemia in whom no evidence of infection was found, and on another who died of meningeal hemorrhage in the course of a relapse, nothing suggestive of bacterial disease was found. The condition presents remissions and relapses analogous to those which occur in pernicious anemia, and in at least one instance[6] a patient has been observed to pass from active anemia into the latent phase.

The chemical variations of the blood and of the urine are similar to those found in other types of hemolytic anemia.

Autopsy findings[7, 8, 9, 10, 11, 12] show degenerative changes in the heart, liver, and kidneys which are referable to the anemia alone in some cases, and in others to anemia plus intercurrent infection. There is also pigmentation of the fat and of the reticulo-

endothelial system. In the liver there is evidence of marked phagocytic activity on the part of the Kupffer cells. The spleens in our active cases have been small, with great fibrosis, partial obliteration of the lymphoid nodules, and great distention of the sinuses with sickle cells. There is abundant pigment deposition in the spleen in the endothelium of the sinuses, in the perivascular connective tissue, and in free macrophages. In 2 cases numerous hemorrhages had occurred into the splenic pulp. The bone-marrow is hyperplastic, numerous nucleated sickle cells are present, and there is abundant pigment.

The treatment of this condition is most unsatisfactory. We felt that by analogy with familial hemolytic icterus, the hemolysis in this disease might be controlled by splenectomy. By some irony of fate we have never been able to secure consent for the operation on one of our cases. In the instances elsewhere where the operation has been performed[2,13,14] there seems to have been relief of anemia, but no effect on the morphology of the blood. It is probable that splenectomy is most effective during the splenomegalic stage of the disease. Liver diet has been tried, in fact, this patient has been on this diet since admission. We have seen no effect from it. Transfusions may serve to tide a severely anemic patient over a critical period, but have no lasting effect.

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## CLINIC OF DR. GROESBECK WALSH

FAIRFIELD, ALABAMA

### THE INDUSTRIAL CLINIC

THE Tennessee Coal, Iron & Railroad Company is a subsidiary of the Steel Corporation. It operates iron mines, coal mines, quarries, and various plants for the manufacture of steel. These plants and mines are grouped around the city of Birmingham, 90 per cent. of them within a radius of 12 miles from the center of the city.

Many of the coal and iron mines are isolated hamlets set off by themselves in the country, frequently being 4 or 5 miles from the nearest community, and exist more or less in a life of their own, the entire adult male population working in the mines, their children attending the Company school, and the families purchasing their food, etc. from commissaries which are conducted at all mines. This description holds good for all of our iron and coal mines, but the industrial plants which are situated in Ensley and Fairfield are not isolated at all, and exist in the suburbs of Birmingham; and the men who work in these industrial plants live either in the suburbs in which the plants are located or in Birmingham itself.

The Tennessee Coal, Iron & Railroad Company employs about 25,000 men, of whom some 65 per cent. are negroes and 35 per cent. are white. There has been in the past ten years a steady increase in the proportion of negro employees. Some fifteen years ago the employees in the coal mines were about equally divided as to white and negro. They are now overwhelmingly negro.

This change took place at about the same time in the ore mines. Probably 90 odd per cent. of the ore and coal miners are of the negro race. The old type of white coal miner who lived in

this district was of English, Scotch, Welsh, and Irish descent. These men were brought up in the mines from childhood and knew nothing of any other means of making a living, and preferred working in coal mines to any other method of employment; but the sons of these men have shown no inclination to take up their father's type of work. So far as the Tennessee Coal, Iron & Railroad Company is concerned, the white miner has almost disappeared.

Owing to the isolated position of many of our communities, such as have been described, it became evident many years ago that some method of medical attention would have to be devised for the workers and families who lived in these places. To supply this need contracts were made with physicians on the basis of so much per man per month. This ranged from $1.00 to $2.00, and was cut out of the employee's wages and given to the physician in a lump sum.

The communities being of considerable size, and in those days health conditions being not what they might have been, a great deal of medical work was necessary. Those physicians that held the original contracts with the company employed men under them at a fixed salary to carry on the medical work under the direction of their immediate chief. Small hospitals were erected by the company to take care of accident work, injuries, minor surgical operations, and occasionally major operations when such seemed necessary. The entire work of the Tennessee Coal, Iron & Railroad Company was divided into some five or six contracts, and entailed before the changes which are to be described took place in the medical department, the employment probably of some 18 or 20 doctors.

It must have been apparent to the most casual observer that the development in the Medical Department and its relation to the employees of the Tennessee Coal, Iron & Railroad Company had not kept pace with the development of other departments. The Tenessee Coal, Iron & Railroad Company at that time was just entering into a period during which the employees, their comfort, their homes, and their general treatment were requiring a great deal more attention than had ever previously been

given them. The very great extent to which the health of the worker and his family entered into his happiness, stability, and desire to remain in one place must have become apparent to the President of the Tennessee Coal, Iron & Railroad Company long before even an inkling of it reached members of the medical department at that time. In fact, it is very doubtful if any such thought ever crossed the minds of those who were doing the medical work.

In 1913 Mr. G. G. Crawford, President of the Tennessee Coal, Iron & Railroad Company, went to the Canal Zone and there selected Dr. Lloyd Noland to come to Birmingham to reorganize and conduct the medical department of the Tennessee Coal, Iron & Railroad Company. The selection was a wise one. Many of the problems to be confronted in Birmingham resembled closely those which the health department had encountered in the Canal Zone. Dr. Noland had been an executive officer of General Gorgas for a time, had been chief of the surgical clinic at Colon Hospital for a number of years, and also superintendent of that institution, and had a wide and varied experience in tropical medicine, sanitation, and hospital management.

It is needless to go into the changes which took place under the new regime. The sanitary work for several years at least became the most important part of the work. Drainage of swamps, eradication of mosquito life, handling of night soil rapidly cut down the incidence of malaria and typhoid fever, so that they became almost negligible, and have remained so until the present time.

The mines and camps were divided into districts placed in charge of district physicians with assistants under them, such as was the vogue in Panama. Efforts were made to standardize the method of work. Reports of sanitary conditions and communicable diseases were made alike in all places, so that they could be handled in the main office without confusion.

Several small hospitals were altered. One of some thirty beds and one of about ten beds were used for surgical patients, selective and otherwise. Such other patients as needed hospitalization were sometimes sent to hospitals in Birmingham.

This method of work of course was very unsatisfactory, although considered a vast improvement over the work which had been previously done.

The period of 1913 to 1918 was one of organization, development of an efficient sanitary department, and eradication of communicable diseases.

In November, 1919 the Employees' Hospital was opened in Fairfield. This hospital, of modern construction in every way, has a capacity of some 300 patients. The staff was selected from our own physicians, with the exception of a few specialists. This staff has been added to since the hospital was opened, and such advancement as has been made in position has been confined to our own people; that is to say, no new blood has been brought into either the medical or surgical department, except that which we have ourselves developed.

The hospital was opened at a time when *x*-ray therapy was just beginning, when the improvement of *x*-ray machines was in its infancy. This department has grown beyond all expectations, occupying at the present time at least four or five times the room originally set apart for it. The physiotherapy department, of which we had not even heard, when the hospital opened, now occupies a section in the hospital almost comparable to that occupied by the *x*-ray department.

Radium has been added, the best type of deep *x*-ray therapy, and every form of physiotherapy, with the exception of hydrotherapy. The hospital contains at the present time as complete an equipment as is likely, I think, to be found in any hospital in America.

In the nine years which have elapsed since the hospital opened, we have developed men to handle the traumatic eye work, the genito-urinary work, obstetrical work, ear, nose, and throat work, and pediatric work. The amount of work which passes through this hospital is capable of developing in individuals, even of most ordinary intelligence, a very considerable degree of skill.

This organization has fulfilled, I think, from the very beginning the purpose for which it was created, and that is to pro-

vide for our employees, who are for the most part of moderate means, a high class medical and surgical service at a price which they could afford. All told this hospital in the nine years during which it has been opened has cared for more than 50,000 patients.

It is probably a very good thing that the Health Department had some means of preparation in the development of men and an opportunity to make a wide acquaintance with the employees of the company before the hospital was opened. It gave opportunity to men in the department to find themselves professionally, and for us to determine to which particular branch they might best devote their time and attention.

One might think that a project of this sort, so largely altruistic in character, would have progressed and succeeded without any opposition whatsoever from any source. Such however has not been the case. One of the most interesting things in the conduct of the Health Department has been the observation of opposition to it, the sources from whence this opposition came, and the way in which it has waxed and waned.

Opposition has come in the main from two groups. One, the employees of this company, our prospective patients; and second, from a very considerable number of the medical profession in the city of Birmingham and its environs. So far as opposition among our own people is concerned, this may be dismissed in a few words. It was, I think, a reflexion on the type of medical and surgical work which had been provided for our employees and their families in the past. We found, even before we opened the hospital, that among a very considerable part of our employees, often the more intelligent, there had developed a decided opposition to the attention of what they called "contract doctors." The men seemed to feel that such medical attention as they would receive from a doctor of this type would be indifferent and would very likely be inefficient. Many of them seemed to feel that if they desired personal attention and interest on the part of the physician, they would have to go outside to physicians who were not on a salary basis with their own company. This was quite generally the attitude of the public mind toward "contract doctors," such as they were fifteen to twenty years ago.

It is very likely that the men working on a small salary, caring for large numbers of people with very scant equipment, with no hospital facilities, with few if any laboratory facilities, could give them, even if the doctor did his very best, but a low grade of medical service. From what I can gather in this district, that is what they did give; and that is the only thing they were able to give with the disadvantages under which they worked.

It took quite a while for us to convince many of our employees, and the convincing I think was done simply by deeds, which proved that we were anxious and able to give to them a quality of medical and surgical attention which compared favorably with anything they could receive elsewhere. Given the facilities with which we now work, the hospital, its remarkable equipment, and its all-time staff, we would be very dull, to say the least, if we could not give this type of attention.

It has been a slow process convincing some, but the some have come to be but a few now; and every year we have had more and more converts. It is true that there are still some people among our employees, very possibly a considerable fraction, who come to us for the sole reason that it costs them less than to go outside. But as time has gone on we are having a very high percentage of readmissions, the people returning to the hospital not grudgingly because it is cheaper, but willingly because they have become convinced that they get here the best return for their money. In certain of our settlements the percentage of men who have gone willingly on the medical fee list, that is, paying in a certain amount every month, has reached 100 per cent., and has shown every sign of remaining at that figure.

Opposition from the other group of individuals, our colleagues in the medical profession, has been a much more serious matter. As long as we confined ourselves to Out Clinic work in the small dispensaries in the various districts and in the operation of two small hospitals, we heard little, if any, criticism of our work, and none at all in any organized way in the State and County Medical Society.

Our hospital here was opened in November, 1919, and all went well until some time in the fall of 1925. Within a period of

a month we were being denounced from all sides very intemperately, and being threatened with loss of our rights as members of the County Medical Society, which, of course, would entail the loss of rights in the State association. The growth of this movement against us was a very interesting thing. It appeared in the open at very short notice, but had been smoldering under cover since the Medical Department of the Tennessee Coal, Iron & Railroad Company was organized.

Conditions in regard to the medical profession in Alabama are closely similar to those in other states. Members of the Jefferson County Medical Society, so far as intelligence and all the standard virtues of their professional life are concerned, compare favorably with that of any similar group in the country.

One could not help feeling, as he watched the opposition to this scheme of medical service develop, that wherever else in the United States similar ideas of organization were put in practice, the same type of opposition would develop and for the same reasons.

At one time the opposition counted in its ranks more than half the members of the Jefferson County Medical Society. Objection to this scheme of medical practice came from all classes and all degrees of intelligence among the members of the Medical Society. It developed, as a matter of course, in that class who felt that their incomes were being impoverished by the extension of our work. This feeling was notably present in the smaller towns where our larger plants were situated, and developed also among many of the members of the Medical Society who had not been particularly successful in building up their practices, and who felt that some form of punitive medical legislation directed against us would automatically increase their incomes. This opposition developed amongst a small but extremely active group who seized this opportunity for elevating themselves to political office in the Medical Society, and to attaining a degree of prominence which they could not possibly have attained, had they not seized this issue as a means of self-elevation. Finally opposition developed among some incorruptible members of the society, who looked upon the scheme of a corporation employing

medical men on a fixed salary and giving all their time and attention to this work, with varying degrees of distrust and suspicion. Added together, this opposition attained considerable impetus. It completely controlled the county politics, and in 1926 at the State meeting in Mobile, it only missed by a very narrow margin forcing its ideas upon the State Association.

What were these ideas, and how did they intend to enforce them? Probably the best way to describe what they had in view is to insert a copy of resolutions which were presented before the Jefferson County Medical Society in the Fall of 1925. They were adopted by a working majority, and were carried down and presented for the consideration of the Alabama State Medical Society in Mobile in the following year.

"Whereas, for a number of years in Jefferson County flagrant and gross violations of the code of ethics of the American Medical Association as well as of the ordinance of the State Medical Association regulating Contract Practice in this State have been known and have been practically ignored by the Jefferson County Medical Society.

"And whereas, all efforts in the past to suppress the growing evil in the profession have failed.

"And whereas, these violations have increased each year to such an extent that the medical profession of Jefferson County has become the object of severe criticism and censure by the profession throughout the State of Alabama and other states.

"And whereas, the high esteem and confidence in which the medical profession has always been held by the public is gradually but surely being lost.

"And whereas, these violations of medical ethics constitute a very grave offense and tend to lower the tone and to destroy the cherished traditions and high ideals of an honorable profession, it becomes imperative that some drastic measures be adopted to arrest this growing menace.

"*Therefore be it Resolved:*

"First: That all list contracts of any character made by any hospital or physician or groups of physicians, mutual aid associations or Insurance Companies of any character providing for medical or surgical services upon the payment of a daily, weekly, monthly, or yearly stipend be declared unethical.

"Second: That it be declared unfair competition and contrary to the ethics of the American Medical Association for any corporation or company who maintains its own hospital to take any patient other than its own employees and their immediate families for hospital medical or surgical services, except accident cases occurring in the vicinity of the hospital.

"Third: That it be declared unethical for any hospital or physician whether paid by the corporation or individual employees to enter into any contract to provide hospital or medical or surgical services upon the payment of a daily, weekly, monthly or yearly stipend, unless the physician or surgeon so employed devotes his entire time to the employees and their families of said corporation. This does not apply to contract for accident cases.

"Fourth: That it is unethical and in violation of the ordinance regulating contract practice in Alabama for any hospital or physician or groups of physicians to enter into contract with corporation, individual, or groups of individuals to furnish hospital medical or surgical services upon payment of a daily, weekly, monthly or yearly stipend, except in accident cases.

"Fifth: That it be declared unethical for any hospital per se to organize a hospital association and enter into any contract with individual or individuals to furnish hospital services on a collection basis, even though they do not agree to furnish the attending physician or surgeon.

"Sixth: That it be declared unethical and in violation of the ordinance regulating contract practice in the State of Alabama for any surgeon or physician employed by any Railroad Company under contract to render medical and surgical services to employees and their families, except in accident cases and then to the employees only.

"Seventh: That it is declared *ethical* and in accordance with the ordinance regulating contract practice in the State of Alabama for a physician to devote his entire time under contract with a mining or manufacturing company to render medical services to its employees and their families. In restricted and outlying areas he may be permitted to do community or outside practice in the immediate vicinity.

"Eighth: That the President of the Jefferson County Medical Society appoint a committee of three whose duty it shall be to co-operate with the Board of Censors in following up this work, and that when any violation of these resolutions be found that the Board of Censors be instructed and given the power to call on the physician or hospital representative where violations are found to exist, and that the Board be empowered to point out wherein violation of these rules regulating contract practice, and if same be not discontinued, that the Board be instructed to report the names of the offenders monthly to the Jefferson County Medical Society in open meeting.

"Ninth: That the Board of Censors be given authority to write letters, employ detectives, summons any physician or hospital representative before it, and have said doctor and hospital representative submit their books and records for inspection.

"Tenth: That all expenses incurred by the Board of Censors and committee in prosecuting this work be borne by the Jefferson County Medical Society.

"Eleventh: That the Board of Censors and committee be instructed to furnish monthly to the Probate Judge in Jefferson County, to the Liability Insurance Companies who are carrying physicians liability insurance, a list of physicians in good standing in the Jefferson County Medical Society.

"Twelfth: That the Secretary of the Jefferson County Medical Society

be instructed to forward a copy of these resolutions to the State Board of Censors and to the State Committee on Contract.

"Thirteenth: That the Board of Censors be requested to take these resolutions under careful attention and consideration and to render a report at the next meeting of the Jefferson County Medical Society, October 23, 1925."

Let us review this resolution without prejudice. I think that all the statements made in the preamble may be accepted at their face value. So far as the resolutions themselves were concerned, it might be said that they took up the question of what is and what is not ethical practice to a degree and to an extent which, so far as I know, has never been taken up before.

In the second paragraph of the resolution a definite effort is made to limit the work of any hospital, but in this instance it referred to the Employees' Hospital of the Tennessee Coal, Iron & Railroad Company, to the treatment of employees and their own immediate families, with the exception of accident cases. Regardless of the rights or wrongs in the matter, and regarding it in a purely judicial way, this is the first attempt of which I am aware that has been made to limit the usefulness of any hospital in this country in such a way.

In the third paragraph of the resolution any physician employed by a company is limited in his practice solely to the care of the employees of the company for which he is working. The ninth and eleventh articles of the resolution combined form together the punitive part of the document. As is well known, it is difficult or impossible for physicians who are not in good standing with the County Medical Society to obtain liability insurance for their practice. So far as the Health Department of the Tennessee Coal, Iron & Railroad Company is concerned, the meat in this cocoanut is confined entirely to two items in the resolution, the first being the effort to restrict the hospital solely to the use of the employees and their immediate families; and the second item that which made it obligatory for any physician employed by a corporation on a whole time basis to confine his attention entirely to the service of the employees and their families.

The idea of how the protagonists of these resolutions intended to enforce them may be found in the eleventh item of the resolutions themselves.

In addition to the resolutions that have been quoted at some length, a second ordinance was introduced at the meeting of the State Medical Society in Mobile in 1926, which was even more particular. In one of its clauses the following rule of conduct was laid down: "A physician may without violating the ethics of the profession practice medicine and surgery for a stated salary for the unskilled or common laborers of a mining or manufacturing company or corporation and the dependent members of their families, but not for the skilled laborers, skilled operators, mechanics, craftsmen, salaried employees, superintendents, managers, and officials of such companies or corporations, or for their families."

This ordinance specified also, for the first time, that a physician upon conviction of violation of this ordinance or any provision thereof, shall be punished by suspension or expulsion from his county medical society.

These various resolutions which had been passed by the Jefferson County Medical Society were reviewed at great length by the State Board of Censors. After a somewhat lengthy preamble an ordinance was enacted.

The two items in the medical service of the Tennessee Coal, Iron & Railroad Company against which the previous resolutions were formulated were treated as follows: In article No. 2 of the ordinance, as presented by the State Board of Censors, they state that a physician, without violating the ethics of his profession, is entitled to perform medical and surgical service for the *unofficial* employees of mining and manufacturing companies and corporations and the dependent members of their families, but not for the salaried officials nor for the families of such salaried officials.

In Article 6 the question of a corporation hospital doing outside work was treated as follows: It is ethical to practice in such a hospital provided said hospital does not enter competitively upon the practice of medicine.

One of the proponents of the original resolutions, which have been quoted before, who was a member of the State Board of Censors, handed in a minority report in which he stated that he could not concur in the report of the majority. This minority report was taken up first in the voting, and was defeated by a vote, which included the counsellors and delegates of the Medical Association of the State of Alabama, of 80 to 75. After a short discussion the majority report of the State Board of Censors, the gist of which has been given above, was adopted unanimously Thus was the matter settled, insofar as it can be settled with two large factions in the medical society possessing such divergent lines of thought.

In 1913, when Dr. Noland had his first conference with Dr. Sanders, then the State Health Officer, a gentleman's agreement was entered into by which the monthly stipend for medical service would be collected from the employees of the Tennessee Coal, Iron & Railroad Company who earned less than $250 per month. This has been adhered to.

It might be said that at the meeting in 1928 the following recommendation regarding this troublesome matter was made by the State Board of Censors, and was unanimously adopted. This is the last official statement concerning this matter by the State Medical Association:

"That the term 'unofficial employee' means any employee, who is not financially able to obtain efficient medical and surgical attention in times of sickness and distress. The employee's income under this interpretation will vary in different parts of the State according to the economics and living conditions in the community in which the particular contract is entered. It is assumed that each country medical society shall have authority to determine the income limit for the contracts within its boundaries, as provided for under the terms of this interpretation. For instance, $150 per month in some communities would be equitable, $200 per month in other communities would be equitable, but in no case, and under no circumstances, and in no locality, shall the income of the employee claiming benefits under

this ordinance exceed, from all his combined sources of revenue, $250 per month or $3000 per annum."

Where the principal point of difference occurred is, of course, in determining just what class of employees should be put on the medical list and be given medical service at reduced rates at the hospital. The second point of difference is the question of the hospital doing outside work. The percentage of non-employees here has been uniformly small, as will be seen from the synopsis of the report for the year 1925:

| | |
|---|---|
| Total patients admitted | 6270 |
| White patients—non-employees | 285 |
| Colored patients—non-employees | 74 |
| Total | 359 |
| Percentage of non-employees admitted | 5.7 |

It will be seen from this synopsis that the percentage of Out Patients is almost negligible; and as repeatedly pointed out in this instance, the constantly increasing number of our employees gives every reason to suppose that this small percentage would be reduced. This fact failed apparently to influence in any way the opposition encountered in the local medical society.

It is remarkable the degree of bitterness this controversy excited. For the past three years it has almost disrupted the Jefferson County Medical Society, and has led to endless bickerings and animosity, which show little, if any, sign of abating. It has been highly complimentary to the Medical Department of the Tennessee Coal, Iron & Railroad Company, and there has been a widespread support in the profession for the character of work it has rendered.

This is only the forerunner, I think, of similar controversies. The physician naturally views the question from his own standpoint, while the corporation which institutes such a medical system and the men who assist in carrying it out very quickly obtain an entirely different point of view from those engaged in general practice. This also is easy to understand. Just what will come of such controversy no one can say. As time goes on, however, despite the opposition of individual physicians, the

number of men engaged in work of this sort in all probability will grow. They, being thoroughly satisfied with the character of medical work which they perform, will of course fight for their position in the County and State Medical Society, feeling that they have done nothing which should cause them to lose such rights.

Judging from the character of the resolutions which were proposed, and which narrowly escaped passing, certain members of the Medical Society believe they have the right to deprive one of his position as a member of the County Medical Society if he does not confirm to their idea of what medical ethics should be. It is undoubtedly true that for various offenses a man may be expelled from a County Medical Society, but on scrutiny these offenses would be found to be offenses primarily against the law of the land or laws of human conduct which would be just as reprehensible outside the medical profession as within it.

Efforts of this description to discipline members of the Medical Society solely on their supposed breech of medical ethics is a new project. To transfer contests between different factions of medical societies over strictly ethical matters to the law courts would subject them to a degree of analysis and criticism to which they have not been exposed before.

Here in this State members of County and State Medical Societies constitute the State Board of Health with definite legal rights. That a society on some so-called ethical ground, which did not involve the question of moral turpitude, could deprive any member of such rights is considered rather doubtful. As pointed out by the late State Health Officer during the argument in the State Medical meeting at Mobile in 1926, if these resolutions had passed in all probability the next step would have been to the courts. Litigation of this sort is prolonged, expensive, and so far as State and County Health and Medical Associations are concerned in the end would I believe, be ruinous. Just what compromise can be worked out remains to be seen.

Since the institution of the Health Department of the Tennessee Coal, Iron & Railroad Company as it at present exists, which has been a matter of some fifteen years, we have had many

more than 1000 applications for positions in the Medical Department of this Company. Resignations from the service are rather infrequent, and so far as can be seen, the majority of the men are contented with the work and the recompense which they receive.

I think it might be stated that the Health Department of the Tennessee Coal, Iron & Railroad Company received the support throughout the whole matter of the late State Health Officer and the majority of the members of the State Board of Health.

It is easily evident that the principles involved in this controversy are applicable to a greater gathering than a county or state medical association. With the growth of industrial medicine, a line of cleavage will be established within the profession, which will set aside a group, ever increasing in numbers, which will view the problem from an entirely different angle than does the individual practitioner.

It is remarkable, after a few years spent in work of this character, how one's point of view diverges from that of those who are in competitive practice. I believe that most of the people who were opposed sincerely to what we were trying to do, that is, opposed in a disinterested way, were perfectly willing to acknowledge that the service we gave our employees was equal to that which they were likely to obtain anywhere in this community; but they felt that it was a rather dangerous innovation for a corporation to employ physicians on an all-time basis with no specifications made, except in a most general way, as to their hours of work, compensation, number of patients they should see daily, etc. In other words, they resented members of the Medical Profession giving up their complete independence; and they took this position not in any way through self-interest, but because they believed it was for the best interest of their group. I was never able to see, even in the most able of our opponents, much evidence that they considered the matter in any light except that of their own trade or guild. In all the controversy, our opponents had little, if anything, to say in regard to the question from the patient's standpoint. I think those who were opposed to us, for

reasons which I have stated above, felt that the work set a precedent, the dangers of which more than counterbalanced the good which our patients received.

They regarded this development as an opening wedge for projects of a similar character, and they felt that in this proceeding members of the profession would frequently be exploited to their own undoing for selfish ends. I think they were perfectly correct in this view. It is exactly what is going to happen, and no doubt has happened. I believe developments along this line will be rapid, and in a decade or so will be fairly widespread. They will be good, bad, and indifferent, just as any medical service today is good, bad, and indifferent. I believe that in certain instances doctors will be overworked, underpaid, and various other forms of injustice will be apparent and easily proved; but I do not believe that such systems of medical care will long survive, if conducted along these lines. In all likelihood the introduction of these methods will be largely through corporations, but there is no question in my mind that the time will come, and shortly, when communities will obtain, if they so desire, group service in a well regulated hospital from competent men at a rate which all can afford.

I think it is only fair to say that the Medical Profession as a whole appears to be opposed to any innovation which threatens their individual independence, no matter how valuable the change may be to the community or to a group consisting of large numbers in any community.

Little criticism of the medical profession becomes articulate, but we know it exists; and one indication is the rapid growth of many cults and isms. Dr. M. L. Harris, writing in the Journal of the American Medical Association, November 26, 1927, states that in the last several examinations for licensure in the state of Illinois the number of chiropractors, osteopaths, etc. exceeded that of the regular profession. He remarks that it is not unreasonable to suppose that there must be some demand on the part of the public for the services of cultists, otherwise there would not be such a large number desiring to enter their ranks.

There is unquestionably a large element of our population,

embracing some of the more intelligent, who view us as a class with a very considerable degree of suspicion. Individuals directing Health Departments of large corporations would, I think, be guided by two considerations. In the first place, the establishment of a center where competent medical and surgical service could be obtained at a reasonable cost; and by a corollary of this the establishment of means to guard the employees and their families from being raided by unscrupulous and incompetent men, many of whom as we know exist within our profession. It is difficult to say which one of these attainments would be more desirable.

To quote again from Dr. M. L. Harris' article of the same date in the Journal American Medical Association where he gives several instances of overcharging for services, one of which is worthwhile quoting verbatim: "The third case is that of a physician who injected a fake and fraudulent so-called serum into a woman who was said to be suffering from a cancer of the stomach. The woman's husband was earning only $147 a month. The doctor charged $300 for this simple injection and, it is alleged, under promise that it would cure his wife, the husband paid his month's check of $147 plus $3 which he borrowed from a neighbor, and gave his note for $150, payable in thirty days, which the doctor at once placed at the bank for collection. He was told not to expect any improvement in his wife for some six weeks or more. As the wife continued to grow worse he refused to pay the note when it became due, but reported the case to the State Board. You will say that this was the work and tactics of a quack, but it wasn't. The doctor was a well-educated physician on the teaching staff of one of our class A universities."

An instance of this description, which seems really authentic, becomes widely known and discussed amongst the laity, and is enough to shake the confidence of intelligent people in the profession as a whole. Whom can they trust? Who is honest and who is dishonest? By what standards, except those of experience, can they be guided in the selection of medical advice? So far as I know, our profession possesses no means whatsoever of disciplining such an individual, or expressing public reproof. Yet,

I believe that multiplying instances of this description have counted more for the lack of confidence in us, which we find so widely scattered throughout the country, than has any other reason. Hampered by the peculiar ethics of our profession, in our silence we connive at this really appalling state of affairs.

The medical profession, I think, has far more than its fair share of rascals. Any profession which is so robed in mystery, so surrounded by all sorts of subterfuges which appeal to those of devious and furtive mind, would inevitably attract and hold individuals of this type.

It has been unfortunate for the medical profession that it is regarded by tradition as a sort of priesthood, working on a plane far above that of the butcher, the baker, the candlestick maker. Removed from the desire to acquire. Above temptation to do anything except that which made the medical tradition what it is. This tradition, as we know, bears very little relation to the facts. Doctors are just like other human beings. They have the same ambitions, the same tastes for luxuries, and the same desire in most instances to meet their ever increasing financial obligations with promptness and honesty.

The old time family practitioner is often held up as a sort of an ideal: The type of man who never sent bills, or sent them only annually. Such an individual would make a pitiful figure in the world as we know it today, and would inevitably end up in the court of bankruptcy.

Those graduating from schools of medicine at the present time very quickly shunt themselves into fields of activity where the return for their work will be prompt and generous. They certainly cannot be blamed for this. We are attempting the very difficult task in our profession of pursuing an altruistic and unselfish ideal in one direction, while busily employed in trying to make as much money as we can by moving sometimes in the opposite way. That is one thing that has made the whole matter so trying, and has cast a semblance of hypocrisy over our acts which, on the whole, I believe is an injustice.

In conclusion I would like to say, that viewed in this light the development of large bodies of men within the medical pro-

fession employed by corporations, states, or cities, opens up a field of endeavor for many to whom the financial side of medicine is repugnant: who, while they possess many of the qualities which go to make fine physicians, stand little, if any, chance in the field of competitive medicine. It is a privilege to practice medicine without the difficulty of viewing every patient we see as a prospective means for the purchase of the necessities or luxuries of life. It is a privilege which once experienced will only be relinguished after a most bitter struggle. I believe that the development of such bodies of men, freed from the temptation of exploiting their patients to their own gain, will raise very materially the plane on which the art of medicine is practised at the present time.

## CLINIC OF DR. FRED W. WILKERSON

MONTGOMERY, ALABAMA

### DIETETIC DIFFICULTIES IN THE SOUTH

MALNUTRITION, not malaria or hookworm, is the curse of the South. Although we have received worldwide notoriety because of the latter two diseases, I venture to state that for every case of either of them there are hundreds of malnutrition, a fact which has not been given sufficient attention. When one studies the question it soon becomes evident that unbalanced dietaries are more responsible for ill health in this section than any other agency. The sallow, scrawny, sluggish individual so often seen in our midst is far more likely to be the sufferer from a deficient diet than from either malaria or hookworm. In fact, a mild hookworm infestation is not incompatible with good health, and I have many times seen individuals harboring a few hookworms derive marked physical improvement from a proper diet, even though they received no hookworm treatment at all.

It is quite likely that the early physical decay of so many rural Southerners is due more to malnutrition than to exposure and hard work, as it is usually thought to be. The men are frequently old beyond their years—their faces seamed, their figures bent, their teeth gone, so that one who is only forty-five may look sixty or sixty-five. This is much more noticeable in the women, who usually by the time they are thirty, have lost all semblance of youth and appear fifteen to twenty years older than they actually are. Hard work and the bearing of children are the factors commonly regarded as responsible, but I believe that close study will reveal malnutrition as equally or more responsible, for many of these women who have not worked hard and have had only one or two children have undergone physical deterioration as

early as their more hard-worked sisters. The more fortunate ones, who have kept their youthful appearance and vigor, as a general rule, will be found to be the ones who have been better fed than the average.

So widespread is the existence of malnutrition that it occurs to the examiner as a possible, even though remote etiologic factor, in almost every patient seen regardless of the actual pathologic condition found. It looms up in the background of practically every case, and we soon learn to study each patient with its possibility in mind. In addition to vitamin deficiency, the examiner often senses a possible mineral deficiency, even though this may be difficult to prove. At times one feels that iodin, arsenic, iron, calcium, or perhaps phosphorus may be lacking, for frequently the diet is deficient in more than one important element.

One of the most difficult things confronting the physician is to find out just what his patients eat. They will tell him with reasonable accuracy the menus served on their tables, but they are extremely vague as to what they themselves actually consume. It is only in comparatively recent years that we have begun to study dietary habits, but now that we are beginning to learn the harmful results of an unbalanced or deficient diet it is important to know in detail the food habits of the patients with whom we deal.

The observations recorded in this paper are the result of several years study of this question in central Alabama. The patients studied were drawn in about equal proportion from rural and urban population. By far the greatest dietetic difficulties are met with in the rural population. In the cities, where access to a good market is possible at all times of the year, our problem is much simpler, but in the country the problem of a proper diet is at times almost insurmountable.

In Alabama and, probably in the other Southern States, there are comparatively few all the year gardens, in spite of the fact that fresh vegetables of some kind can be grown the year round. Reliable authorities estimate that only 50 per cent. of the farm families of the state have an adequate milk supply, and that

poultry and eggs are not included in the diet to the extent that they should be. Many farmers who do have cows and chickens sell their milk and eggs, thus depriving their own families of these valuable foods. It is impossible in the small towns and country districts to have vegetables shipped from the markets, so that those without their own gardens are forced through a large part of the year to do without these necessary foods. Oftentimes co-operative patients will write that they have been unable to follow directions because of the utter impossibility of getting fresh vegetables, milk, eggs, or whatever else may have been prescribed. This situation exists too, not only among the poorer classes of Southern Country folk, but among many in good circumstances.

Many of our Southern country people live throughout the winter on a diet of white flour bread and corn bread, potatoes, syrup, and some form of pork, more frequently salted pork. Just here let it be said that to the average rural Alabamian the terms "meat" and "pork" are synonymous. When speaking of meat he refers only to pork, so his actual consumption of beef, chicken, or other meat will not be discovered unless specific inquiry is made. There may be, in addition, more or less of the highly milled cereals, eggs, a small amount of milk, and jams, jelly or preserves, as a rule made by a process which destroys all vitamin content of the fruit. There is a tendency in many households to have two or three kinds of bread and several kinds of meat at the same meal. Thus corn bread, biscuit, and light-bread, steak, ham, and fresh pork I have often seen at one meal and this same meal three times a day even in better class country homes. No fresh vegetables, no fruits and an insufficient supply of milk or milk products.

Too many farm families are buying their food from the country store, instead of raising essentials, as they so easily might. It is manifest at a glance how lacking is such a dietary. This is bad enough for the adults, but when it is realized that the children who pattern after their parents' food habits and acquire their food likes and dislikes very young, are reared on such diets, it becomes a matter of serious moment. Of course, this unbalanced

and insufficient ration is not universal, but it is altogether too prevalent and prevails, perhaps, in the majority of rural homes. The caloric value is usually ample, and at times of the year there is a plentiful supply of fresh vegetables, fresh fruit, and fresh milk, but this is woefully inadequate except during early spring and summer.

Dickins, in a study of the food habits of 100 representative families from two different areas of Mississippi, summarizes practically as follows: (1) That scarcely more than was actually necessary of energy protein and phosphorus was well provided; that calcium was well provided; that iron was not provided in sufficient quantities; that vitamin A and B requirements were probably met, and that vitamin C was low in fall, winter, and early spring.

(2) Little seasonal variation in the nutritive values of these Mississippi dietaries was found.

(3) The average number of physical defects per child per family was higher for the families whose dietaries were below standard in two or more nutritional factors.

These conclusions probably accord closely with the average in the Southern States, except that in many instances the supply of calcium is insufficient for the growing child, due to the small amount of milk taken by so many children. In my observation not many children get the quart of milk a day which is supposed to be the minimum amount necessary for adequate growth.

The effect of unbalanced, insufficient diets has not been seriously enough considered by the profession as a whole. Of course, the definite deficiency diseases, such as rickets, scurvy, and possibly pellagra, have been thoroughly studied and their relation to food is well known. But it is extremely likely that there are many "vague more or less indefinite states of malnutrition" and ill health resulting from dietary insufficiency that are not recognized. There is a type of individual seen in the South, usually sallow, with dry, harsh skin, often underweight, lethargic, complaining constantly of "biliousness" or "malaria," resorting to calomel frequently, going from one doctor to another without relief, who will improve promptly when put on a diet containing green

vegetables, fruits, and milk in abundance—undoubtedly a victim of dietary deficiency.

The majority who live on the diet described are constipated, many of them have sour stomach, heartburn, flatulence, and oftentimes the symptoms simulate gall-bladder disease, duodenal ulcer, or chronic appendicitis so that quite frequently they are operated on for one or the other of those conditions, of course, without improvement. This comes only when the dietary deficiency is recognized and a proper regimen is instituted.

The maxim, "a clean tooth never decays" is in need of revision for it is now recognized that dietary deficiency, particularly of calcium, plays an important rôle in dental caries. The evidence that calcium and vitamin deficiency do play such a rôle is steadily increasing, and it is an unquestioned fact that many people who take scrupulous care of their teeth yet suffer from decaying teeth. In my observation these have been the people who eat heavily of carbohydrates at the expense of green vegetables. May this not partially explain the tremendous amount of tooth decay in Southern Country people? It is rare not to find one or more decayed teeth in the mouth of nearly every rural Southern child and the amount of decay among the adults of this section is astounding.

The diet and the cooking of our people probably go far toward explaining the coated tongue and the frequent complaint of "biliousness," both more common than in other parts of the country. The periodic use of calomel both by the profession and the laity is well nigh universal, so that the majority of people think 3 or 4 doses of the mild chlorid of mercury a year are necessary for well being and health. The doctor who looks with disfavor on so much mercury and advises, instead, a change of diet is distrusted by many accustomed to the old order of things. The wonder is that there is not more disabling gastro-intestinal disease than there is.

The inability of our rural patients to procure the needed foods throughout the year is our greatest dietetic difficulty, but there are others of great importance, not the least of which is the poor cooking in the homes of the majority. Our much vaunted South-

ern cooking deserves all its reputation, but, unfortunately, this excellence in the culinary art is confined to the few. It is a distressing thing to see good material ruined in its preparation, yet wretched cooking is a daily occurrence, even in many homes of the well-to-do. Vegetables are greasy, poorly flavored, often cooked too long. The bread is heavy and soggy. Many housewives can only fry and boil meat, and the end product is usually swimming in grease. The chief food dislike among children is for green vegetables and this distaste is acquired very early in life. The explanation, I think, is to be found in the miserable way in which the vegetables are prepared. The vitamin content of many of the leafy vegetables is probably destroyed by the long boiling to which they are so often subjected, so that even during seasons of the year when vegetables are plentiful, there may be a vitamin deficiency just the same.

Several years ago I was consulted by a rural physician, who had such severe digestive trouble that his condition had been diagnosed as gastric cancer. Study of his case revealed clearly that it was one of dietary indiscretion rather than malignancy, and improvement followed institution of a better diet, but even then the symptoms persisted to a certain extent. Several months after I first saw him I had occasion to take a meal in his home and it became apparent at once why his trouble was not cured. He was eating the right things, but they were cooked in the manner just described. The vegetables were greasy, the biscuits heavy and soggy, and a large dish of fried chicken, swimming in grease was the *piece de resistance*. He ate heavily not only of the solid food, but took with the greatest relish spoonful after spoonful of the greasy gravy. After the meal I called him aside, made due apologies for being critical, and showed him the utter impossibility of recovery on such food. Fortunately he realized the justice of the criticism, instituted the necessary changes, his trouble cleared up, and has not since recurred.

Food such as pictured is all too prevalent among people able and intelligent enough to know better and is well nigh universal among the masses in the rural South. Unfortunately, too, they like it that way. They have been reared on it and they do not

want it prepared otherwise, which adds greatly to our difficulty in correcting the error. The author of the statement that many a man would recover from indigestion if he would only change his cook, must have lived or travelled in the South.

Another difficulty is that so many housewives do not know how to plan a menu or how to make the food attractive looking. There is too much monotomy in the diet. Very little variation is found from day to day or from meal to meal. One frequently sees breakfast, dinner, and supper identical, day in and day out so that even if properly prepared it palls because of its sameness. There is oftentimes a shocking waste of foodstuffs, a factor of importance to many of these families who can ill afford it. Two or three kinds of meat, two or three kinds of bread, potatoes, rice, grits, at the same meal. All this means a not inconsiderable useless expense to a family when kept up constantly. Habit is a difficult thing to overcome, however.

Treatment of these cases, particularly in the adults, is likely to be difficult because of the length of time often required for improvement. It is no easy matter to change faulty food habits of many years' standing. Restoration to the normal is necessarily slow in coming about where processes have been perverted for so many years. Tact, patience, and persistence are necessary in overcoming fixed food prejudices and much diplomacy must be used to effect the desired dietary changes. Most of these patients will take gladly all the medicines given, but persuading them to eat things they do not like and are not accustomed to is another matter. Success depends on the ability of the doctor to convince his patient, a task by no means always easy. One successful case in a family often means an improved dietary for the whole family, for a father or mother restored to health and taught the essentials of diet, will see that the other members of the household have the same food.

Children are usually not as difficult to handle as adults, for their food habits, more recently acquired, are more easily changed. If the mother is co-operative, astounding results can be achieved in the young in a comparatively short time. The pediatrists of the South have done wonderful work in educating mothers as to

the dietary needs of their children and this has helped to make the handling of adults a far less difficult problem than was the case even fifteen years ago.

The remedy for our situation is easy to know, but difficult to apply. In the first place we should begin with the profession itself for most of us have paid too little attention to this important phase of our work. The State Boards of Health and the various Extension Departments of our State Schools are doing a great deal of good work in educating the laity, but after all, the individual physician is the man who bears the chief responsibility. He gets closest to his patients and they value his counsel more than that of any one else. Not until he takes a serious enough interest in dietetic problems to advise his patients properly will a great deal of headway be made.

It is not enough to take a diet slip from a text-book and give it to a patient. One must know what foods are available to the particular patient, construct his list, from them, and teach the patient how to use them. Most of our text-books on diets have been written by Northern writers and many foodstuffs in their lists are not available to our Southern people, yet there is no time of the year when all necessary food elements are not obtainable in this section. We should preach to the people the need for year round gardens, and the advisability of raising more of their foodstuffs than they do at present. The Southern diet in the summer should consist almost entirely of milk and milk products, raw and cooked vegetables, raw fruits, bread, and a minimum amount of meat. The necessary protein can be obtained from the milk and a small amount of meat, while all the other necessary factors will be yielded by the vegetables, fruit, and bread. In the winter more meat and eggs, cereals, desserts, and nuts can be added, but even then vegetables, fruit, and milk should constitute the bulk of the food. Our Southern barbecue, delightful as it is, is really a bad institution. The rich camp stew, the barbecued meats are truly delightful to the taste, but they are winter time foods and should not be eaten in the summer, the time of year at which barbecues are generally held.

We should not only try to teach our patients to be more

"vegetable, fruit, and milk minded," but should try to give them some instructions as to cooking and varying their menus. Not many physicians are culinary experts, but we can at least instruct housewives as to the harm of greasy food, of improper seasoning, and as to proper combinations of food. We can teach them the value of a varied diet and instruct them as to making their dishes palatable and attractive. Concerted effort along these lines by the majority of Southern physicians would in the course of a few years cause great improvement in dietary habits, with a consequent increase in the well being of our population. No radical change is to be expected, however, because the profession itself does not yet fully realize the situation. All educational processes work slowly, but once the profession goes seriously into this problem, spreads the doctrine of vegetables, fruits, and milk as the mainstay of our diet, and works diligently to change the improper food habits of our people, improvement is bound to occur. Not a great deal can be accomplished for the present generation, but the next twenty-five years should see as great an advance in this phase of our work as there has been in other branches of medicine in the last quarter of a century.